

(19)



Europäisches Patentamt  
European Patent Office  
Office européen des brevets



(11)

**EP 1 088 899 A2**

(12)

**EUROPEAN PATENT APPLICATION**

(43) Date of publication:

**04.04.2001 Bulletin 2001/14**

(51) Int Cl.7: **C12Q 1/68**

(21) Application number: **01200037.8**

(22) Date of filing: **23.06.1995**

(84) Designated Contracting States:

**AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL  
PT SE**

Designated Extension States:

**LT LV SI**

(30) Priority: **24.06.1994 EP 94870106**

**07.04.1995 EP 95870032**

(62) Document number(s) of the earlier application(s) in  
accordance with Art. 76 EPC:

**95924923.6 / 0 769 068**

(71) Applicant: **N.V. INNOGENETICS S.A.**

**9052 Gent (BE)**

(72) Inventors:

- **Jannes, Geert**  
**3010 Kessel-Lo (BE)**
- **Rossau, Rudi**  
**2180 Ekeren (BE)**
- **Van Heuverswyn, Hugo**  
**9270 Kalken (BE)**

Remarks:

This application was filed on 08 - 01 - 2001 as a  
divisional application to the application mentioned  
under INID code 62.

(54) **Simultaneous detection, identification and differentiation of Eubacterial taxa using a  
hybridization assay**

(57) The present invention relates to a method for  
detection and identification of at least one micro-organ-  
ism, or for the simultaneous detection of several micro-  
organisms in a sample, comprising the steps of:

- (i) if need be releasing, isolating or concentrating  
the polynucleic acids present in the sample;
- (ii) if need be amplifying the 16S-23S rRNA spacer  
region, or a part of it, with at least one suitable prim-  
er pair;
- (iii) hybridizing the polynucleic acids of step (i) or (ii)  
with at least one and preferably more than one of  
the spacer probes as mentioned in table Ia or equiv-  
alents of thereof, under the appropriate hybridization

and wash conditions, and/or with a taxon-specific  
probe derived from any of the spacer sequences as  
represented in figs. 1-103 under the same hybridi-  
zation and wash conditions;

(iv) detecting the hybrids formed in step (iii) with  
each of the probes used under appropriate hybridi-  
zation and wash conditions;

(v) identification of the micro-organism(s) present  
in the sample from the differential hybridization sig-  
nals obtained in step (iv).

**EP 1 088 899 A2**

## Description

[0001] The present invention relates to nucleic acid probes derived from the spacer region between the 16S and 23S ribosomal ribonucleic acid (rRNA) genes, to be used for the specific detection of eubacterial organisms in a biological sample by a hybridization procedure, as well as to nucleic acid primers to be used for the amplification of said spacer region of eubacterial organisms in a biological sample. The present invention also relates to new spacer region sequences from which said probes or primers may be derived.

[0002] Since the advent of the polymerase chain reaction and some other nucleic acid amplification techniques the impact of DNA-probe technology in the diagnosis of micro-organisms in biological samples of all sorts is increasing. Being often more specific and potentially more sensitive - if an adequate amplification and/or detection system is used - the DNA probe approach may eventually replace the conventional identification techniques.

[0003] The reliability of nucleic acid based tests essentially depends on the sensitivity and specificity of the probes and/or primers used. Thus the corner stone of this type of assay is the identification of nucleic acid sequences which are unique to the group of organisms of interest.

[0004] Most of the nucleic acid based tests either described in literature and/or commercially available aim at the detection of just one particular organism in a biological sample. Since most biological samples usually may contain a great variety of clinically relevant micro-organisms, a multitude of separate assays have to be performed to detect all relevant organisms possibly present. This approach would be very expensive, laborious and time-consuming. Consequently, the number of tests actually performed in most routine diagnostic labs on a particular sample is restricted to the detection of just a few of the most relevant organisms. Therefore it would be extremely convenient to have access to a system which enables the fast, easy and simultaneous detection of a multitude of different organisms. The more organisms that can be screened for in the same assay, the more cost-effective the procedure would be.

[0005] As put forward in earlier published documents, the spacer region situated between the 16S rRNA and the 23S rRNA gene, also referred to as the internal transcribed spacer (ITS), is an advantageous target region for probe development for detection of pathogens of bacterial origin (International application WO 91/16454; Rossau et al., 1992; EP-A-0 395 292).

[0006] One of its most appreciated advantages is that sequences unique to a great variety of bacterial taxa can be found in a very limited area of the bacterial genome. This characteristic allows for an advantageous design of "probe-panels" enabling the simultaneous detection of a set of organisms possibly present in a particular type of a biological sample. Moreover, being flanked by quasi-universally conserved nucleotide sequences - more particularly located in the 3'-part of the 16S rRNA gene and the 5'-part of the 23S rRNA gene respectively - almost all spacers can be simultaneously amplified with a limited set of amplification primers. Alternatively, specific primer sets can be derived from the spacer sequences themselves, thereby allowing species- or group-specific amplifications.

[0007] The 16S-23S rRNA spacer region is a relatively short (about 200 to 1000 base pairs) stretch of DNA present in one or multiple copies in the genome of almost all eubacterial organisms. If multiple copies are present in the genome of one bacterium these copies can either be identical (as is most probably the case in some *Neisseria* species) or may differ from each other (as is the case for *E. coli*). This difference can be limited to a few nucleotides but also deletions and insertions of considerable length may be present.

[0008] Uptil now, spacer probes are only described and made publicly available for a limited number of organisms many of which were disclosed in international application WO 91/16454. As described above, it would be very advantageous to be able to detect simultaneously a panel of pathogens: e.g. a panel of pathogens possibly present in the same type of biological sample, or a panel of pathogens possibly causing the same type of disease symptoms, which are difficult to differentiate clinically and/or biochemically, or a panel of organisms belonging to the same taxon. In order to make the different panels as complete as possible, additional probes or sets of probes located in the spacer region and enabling the identification of at least the following bacterial groups or species are required:

- Mycobacterium species
- Listeria species
- Chlamydia species
- Acinetobacter species
- Mycoplasma species
- Streptococcus species
- Staphylococcus species
- Salmonella species
- Brucella species
- Yersinia species
- Pseudomonas species

[0009] These additional spacer probes need to be meticulously designed such that they can be used simultaneously with at least one other probe, under the same hybridization and wash conditions, allowing the detection of a particular panel of organisms.

[0010] It is thus the aim of the present invention to select probes or sets of probes, which have as target the 16S-23S rRNA spacer region, and which allow the detection and identification of at least one, and preferably more than one, of the above mentioned micro-organisms. The probes or probe sets are selected in such a way that they can be used in combination with at least one other probe, preferably also originating from the 16S-23S rRNA spacer region, under the same hybridisation and wash conditions, to allow possibly the simultaneous detection of several micro-organisms in a sample.

[0011] It is also an aim of the present invention to provide for a selection method for use in the selection of said spacer probes or probe sets.

[0012] It is also an aim of the present invention to provide a rapid and reliable hybridization method for detection and identification of at least one micro-organism in a sample, or for the simultaneous detection and identification of several micro-organisms in a sample.

[0013] It is more particularly an aim of the present invention to provide a hybridization method allowing simultaneous detection and identification of a set of micro-organisms, liable to be present in a particular type of sample.

[0014] It is more particularly an aim of the present invention to provide probes or sets of probes for the possible simultaneous detection of micro-organisms in a sample originating from respiratory tract.

[0015] It is another particular aim of the present invention to provide probes or sets of probes for the possible simultaneous detection of micro-organisms in a sample originating from cerebrospinal fluid.

[0016] It is still another particular aim of the present invention to provide probes or sets of probes for the possible simultaneous detection of micro-organisms in a sample originating from urogenital tract.

[0017] It is still another particular aim of the present invention to provide probes or sets of probes for the possible simultaneous detection of micro-organisms in a sample taken from the gastro-intestinal tract of a patient.

[0018] It is still another particular aim of the present invention to provide probes or sets of probes for the possible simultaneous detection of micro-organisms in a sample originating from food or environmental samples.

[0019] It is moreover an aim of the present invention to provide a method for detection and identification of a particular taxon in a sample, or a set of particular taxa, said taxon being either a complete genus, or a subgroup within a genus, a species or even subtypes within a species (subspecies, serovars, sequevars, biovars...).

[0020] It is more particularly an aim of the present invention to provide probes or sets of probes for the detection of Mycobacterium species and subspecies, more particularly for the detection of M. tuberculosis complex strains, Mycobacterium strains from the MAIS-complex, M. avium and M. paratuberculosis, M. intracellulare and M. intracellulare-like strains, M. scrofulaceum, M. kansasii, M. chelonae, M. goodii, M. ulcerans, M. genavense, M. xenopi, M. simiae, M. fortuitum, M. malmoense, M. celatum and M. haemophilum.

[0021] It is also an aim of the present invention to provide probes or sets of probes for the detection of Mycoplasma strains, more particularly of M. pneumoniae and M. genitalium.

[0022] It is also an aim of the present invention to provide probes or sets of probes for the detection of Pseudomonas strains, more particularly P. aeruginosa.

[0023] It is also an aim of the present invention to provide probes or sets of probes for detection of Staphylococcus species, more particularly S. aureus and S. epidermidis.

[0024] It is also an aim of the present invention to provide probes or sets of probes for the detection of Acinetobacter strains, more particularly A. baumannii.

[0025] It is also an aim of the present invention to provide probes or sets of probes for the detection of Listeria strains, more particularly Listeria monocytogenes.

[0026] It is also an aim of the present invention to provide probes or sets of probes for the detection of Brucella strains.

[0027] It is also an aim of the present invention to provide probes or sets of probes for the detection of Salmonella strains.

[0028] It is also an aim of the present invention to provide probes or sets of probes for the detection of Chlamydia strains, more particularly C. trachomatis and C. psittaci.

[0029] It is also an aim of the present invention to provide probes or sets of probes for the detection of Streptococcus strains.

[0030] It is also an aim of the present invention to provide probes or sets of probes for the detection of Yersinia enterocolitica strains.

[0031] It is also an aim of the present invention to provide primers allowing specific amplification of the 16S-23S rRNA spacer region for certain organisms. More particularly, it is an aim of the present invention to provide primers for the specific amplification of the spacer region of Mycobacterium, Chlamydia, Listeria, Brucella and Yersinia enterocolitica strains.

[0032] It is also an aim of the present invention to provide new sequences of 16S-23S rRNA spacer regions from

which useful spacer probes or primers can be derived.

**[0033]** It is also an aim of the present invention to provide for kits for detection of at least one organism in a sample in which said probes and/or primers are used.

**[0034]** It is noted that for a few of the above-mentioned organisms spacer sequences have already been published in literature or in publicly accessible data-banks.

**[0035]** However, it should be made clear that the spacer region sequences disclosed in the current invention (figs. 1-103) are new and, in case they originate from the same species as those of which a spacer sequence was already described in the prior art, they differ to some extent from the already described sequences.

**[0036]** Moreover, it is the principal aim of the present invention to select, from the compilation of sequence data on spacer regions, specific probes and sets of probes enabling the detection and identification of a particular panel of organisms, be it the organisms belonging to a common taxon, or the organisms possibly present in the same type of sample.

**[0037]** The selection procedure usually consists of a theoretical and an experimental part. First of all, the different spacer sequences need to be aligned to those of the 'closest neighbours' or to the spacer sequences of other micro-organisms liable to be present in the same sample. This requires of course the sequence determination of the spacer region, as described in the examples. From the alignment, regions of divergence can be defined, from which probes with desired hybridization characteristics are designed, according to guidelines known to the man skilled in the art and specified in more detail below.

**[0038]** Secondly, the designed probes need to be tested experimentally and evaluated for their usefulness under specific hybridization conditions and/or in combination with other probes. Experimental testing can be done according to any hybridization method known in the art, but a preferred assay for the simultaneous testing of different probes under the same conditions is the reverse hybridization assay. A specific format for reverse hybridization of different probes simultaneously used in the current invention is the LiPA (Line Probe Assay) as described below.

**[0039]** Upon experimental testing unexpected hybridization behaviour may show up when the probes are hybridized to the target nucleic acid, and specific probe adaptations may be required.

**[0040]** Moreover, specificity and sensitivity of the probes need to be tested with a large collection of strains, both belonging to the taxon to be detected and belonging to other taxa. Due to genome heterogeneity in the spacer region, or the existence of multiple spacer regions with different sequences in the same organism, it is quite often necessary to sequence spacer regions of additional strains, or to sequence additional spacer regions in the same strain, and redesign the probes according to the new sequence data in order to obtain a better sensitivity and/or specificity (see e.g. example 3). In some cases it may be necessary or preferable to use several probes for the same organism (see e.g. example 2 and 7). Also, upon sequencing the spacer region, some organisms may show unexpected (un)relatedness, which may lead to a revision of strain classification contrary to classical taxonomic criteria (see e.g. examples 2 and 7).

**[0041]** In conclusion, the experimental part of the probe selection procedure is indispensable and complementary to the theoretical part. Probe design, especially under the fixed conditions of reverse hybridization (the same conditions for each probe) is not straightforward and probes have to be evaluated meticulously before they can be used in a reverse hybridization format. Therefore, probes cannot always be simply derived on a theoretical basis from a known gene sequence.

**[0042]** For designing probes with desired characteristics the following useful guidelines may be followed.

**[0043]** Because the extent and specificity of hybridization reactions such as those described herein are affected by a number of factors, manipulation of one or more of those factors will determine the exact sensitivity and specificity of a particular probe, whether perfectly complementary to its target or not. The importance and effect of various assay conditions, explained further herein, are known to those skilled in the art.

**[0044]** First, the stability of the [probe : target] nucleic acid hybrid should be chosen to be compatible with the assay conditions. This may be accomplished by avoiding long A and T rich sequences, by terminating the hybrids with G:C base pairs, and by designing the probe with an appropriate T<sub>m</sub>. The beginning and end points of the probe should be chosen so that the length and %GC result in a T<sub>m</sub> about 2-10°C higher than the temperature at which the final assay will be performed. The base composition of the probe is significant because G-C base pairs exhibit greater thermal stability as compared to A-T base pairs due to additional hydrogen bonding. Thus, hybridization involving complementary nucleic acids of higher G-C content will be stable at higher temperatures.

**[0045]** Conditions such as ionic strength and incubation temperature under which a probe will be used should also be taken into account in constructing a probe. It is known that hybridization will increase as the ionic strength of the reaction mixture increases, and that the thermal stability of the hybrids will increase with increasing ionic strength. On the other hand, chemical reagents, such as formamide, urea, DMSO and alcohols, which disrupt hydrogen bonds, will increase the stringency of hybridization. Destabilization of the hydrogen bonds by such reagents can greatly reduce the T<sub>m</sub>. In general, optimal hybridization for synthetic oligonucleotide probes of about 10-50 bases in length occurs approximately 5°C below the melting temperature for a given duplex. Incubation at temperatures below the optimum



may allow mismatched base sequences to hybridize and can therefore result in reduced specificity.

[0046] It is desirable to have probes which hybridize only under conditions of high stringency. Under high stringency conditions only highly complementary nucleic acid hybrids will form; hybrids without a sufficient degree of complementarity will not form. Accordingly, the stringency of the assay conditions determines the amount of complementarity needed between two nucleic acid strands forming a hybrid. Stringency is chosen to maximize the difference in stability between the hybrid formed with the target and the nontarget nucleic acid. In some examples of the current invention, e.g. when highly related organisms need to be differentiated, it may be necessary to detect single base pair changes. In those cases, conditions of very high stringency are needed.

[0047] Second, probes should be positioned so as to minimize the stability of the [probe : nontarget] nucleic acid hybrid. This may be accomplished by minimizing the length of perfect complementarity to non-target organisms, avoiding GC rich regions of homology to non-target sequences, and by positioning the probe to span as many destabilizing mismatches as possible. Whether a probe sequence is useful to detect only a specific type of organism depends largely on the thermal stability difference between [probe:target] hybrids and [probe:nontarget] hybrids. In designing probes, the differences in these  $T_m$  values should be as large as possible (e.g. at least 2°C and preferably 5°C).

[0048] The length of the target nucleic acid sequence and, accordingly, the length of the probe sequence can also be important. In some cases, there may be several sequences from a particular region, varying in location and length, which will yield probes with the desired hybridization characteristics. In other cases, one sequence may be significantly better than another which differs merely by a single base. While it is possible for nucleic acids that are not perfectly complementary to hybridize, the longest stretch of perfectly complementary base sequence will normally primarily determine hybrid stability. While oligonucleotide probes of different lengths and base composition may be used, oligonucleotide probes preferred in this invention are between about 10 to 50 bases in length and are sufficiently homologous to the target nucleic acid.

[0049] Third, regions in the target DNA or RNA which are known to form strong internal structures inhibitory to hybridization are less preferred. Likewise, probes with extensive self-complementarity should be avoided. As explained above, hybridization is the association of two single strands of complementary nucleic acids to form a hydrogen bonded double strand. It is implicit that if one of the two strands is wholly or partially involved in a hybrid that it will be less able to participate in formation of a new hybrid. There can be intramolecular and intermolecular hybrids formed within the molecules of one type of probe if there is sufficient self complementarity. Such structures can be avoided through careful probe design. By designing a probe so that a substantial portion of the sequence of interest is single stranded, the rate and extent of hybridization may be greatly increased. Computer programs are available to search for this type of interaction. However, in certain instances, it may not be possible to avoid this type of interaction.

[0050] The probes of the present invention are designed for attaining optimal performance under the same hybridization conditions so that they can be used in sets for simultaneous hybridization; this highly increases the usability of these probes and results in a significant gain in time and labour. Evidently, when other hybridization conditions should be preferred, all probes should be adapted accordingly by adding or deleting a number of nucleotides at their extremities. It should be understood that these concomitant adaptations should give rise to essentially the same result, namely that the respective probes still hybridize specifically with the defined target. Such adaptations might also be necessary if the amplified material should be RNA in nature and not DNA as in the case for the NASBA system.

[0051] The hybridization conditions can be monitored relying upon several parameters, such as the nature and concentration of the components of the media, and the temperatures under which the hybrids are formed and washed.

[0052] The hybridization and wash temperature is limited in upper value depending on the sequence of the probe (its nucleic acid composition, kind and length). The maximum hybridization or wash temperature of the probes described in the present invention ranges from 40°C to 60°C, more preferably from 45°C to 55°C, in the specific hybridization and wash media as described in the Examples section. At higher temperatures duplexing (= formation of the hybrids) competes with the dissociation (or denaturation) of the hybrid formed between the probe and the target.

[0053] In a preferred hybridization medium of the invention, containing 3 x SSC and 20% formamide, hybridization temperatures can range from 45°C to 55°C, with a preferred hybridization temperature of 50°C. A preferred wash medium contains 3 x SSC and 20% formamide, and preferred wash temperatures are the same as the preferred hybridization temperatures, i.e. preferably between 45°C and 55°C, and most preferably 50°C.

[0054] However, when modifications are introduced, be it either in the probes or in the media, the temperatures at which the probes can be used to obtain the required specificity should be changed according to known relationships, such as those described in the following reference: Hames B and Higgins S (eds.). Nucleic acid hybridization. A practical approach, IRL Press, Oxford, U.K., 1985.

[0055] The selected nucleic acid probes derived from the 16S-23S rRNA spacer region and described by the present invention are listed in Table Ia (SEQ ID NO 1 to 64, 175 to 191, 193 to 201, and 210 to 212). As described in the examples section, some of these probes show a better sensitivity and/or specificity than others, and the better probes are therefore preferentially used in methods to detect the organism of interest in a biological sample. However, it is possible that for certain applications (e.g. epidemiology, substrain typing, ...) a set of probes including the less specific

and/or less sensitive probes may be very informative (see e.g. example 7).

**[0056]** The following definitions serve to illustrate the terms and expressions used in the different embodiments of the present invention as set out below.

**[0057]** The term "spacer" is an abbreviated term referring to the 16S-23S rRNA internal transcribed spacer region.

5 **[0058]** The term "probe" refers to single stranded sequence-specific oligonucleotides which have a sequence which is sufficiently complementary to hybridize to the target sequence to be detected.

**[0059]** The more specific term "spacer probe" refers to a probe as defined above having a sequence which is sufficiently complementary to hybridize to a target sequence which is located in the spacer region(s) of the organism (or group of organisms) to be detected.

10 **[0060]** Preferably said probes are 70%, 80%, 90%, or more than 95% homologous to the exact complement of the target sequence to be detected. These target sequences are either genomic DNA or precursor RNA, or amplified versions thereof.

**[0061]** Preferably, these probes are about 5 to 50 nucleotides long, more preferably from about 10 to 25 nucleotides. The nucleotides as used in the present invention may be ribonucleotides, deoxyribonucleotides and modified nucleotides such as inosine or nucleotides containing modified groups which do not essentially alter their hybridization characteristics. Moreover, it is obvious to the man skilled in the art that any of the below-specified probes can be used as such, or in their complementary form, or in their RNA form (wherein T is replaced by U).

15 **[0062]** The probes according to the invention can be formed by cloning of recombinant plasmids containing inserts including the corresponding nucleotide sequences, if need be by cleaving the latter out from the cloned plasmids upon using the adequate nucleases and recovering them, e.g. by fractionation according to molecular weight. The probes according to the present invention can also be synthesized chemically, for instance by the conventional phosphotriester method.

**[0063]** The term "complementary" nucleic acids as used herein means that the nucleic acid sequences can form a perfect base-paired double helix with each other.

25 **[0064]** The term "homologous" as used in the current application is synonymous for identical: this means that polynucleic acids which are said to be e.g. 80% homologous show 80% identical base pairs in the same position upon alignment of the sequences.

**[0065]** The term "polynucleic acid" corresponds to either double-stranded or single-stranded cDNA or genomic DNA or RNA, containing at least 10, 20, 30, 40 or 50 contiguous nucleotides. A polynucleic acid which is smaller than 100 nucleotides in length is often also referred to as an oligonucleotide. Single stranded polynucleic acid sequences are always represented in the current invention from the 5' end to the 3' end.

**[0066]** The term 'closest neighbour' means the taxon which is known or expected to be most closely related in terms of DNA homology and which has to be differentiated from the organism of interest.

35 **[0067]** The expression 'desired hybridization characteristics' means that the probe only hybridizes to the DNA or RNA from organisms for which it was designed, and not to DNA or RNA from other organisms (closest neighbours or organisms liable to be present in the same sample). In practice, this means that the intensity of the hybridization signal is at least two, three, four, five, ten or more times stronger with the target DNA or RNA from the organisms for which the probes were designed, as compared to non-target sequences.

**[0068]** These desired hybridization characteristics correspond to what is called later in the text "specific hybridization".

40 **[0069]** The expression "taxon-specific hybridization" or "taxon-specific probe" means that the probe only hybridizes to the DNA or RNA from the taxon for which it was designed and not to DNA or RNA from other taxa.

**[0070]** The term taxon can refer to a complete genus or a sub-group within a genus, a species or even subtype within a species (subspecies, serovars, sequevars, biovars...).

45 **[0071]** The term "specific amplification" or "specific primers" refers to the fact that said primers only amplify the spacer region from these organisms for which they were designed, and not from other organisms.

**[0072]** The term "sensitivity" refers to the number of false negatives: i.e. if 1 of the 100 strains to be detected is missed out, the test shows a sensitivity of  $(100-1/100)\% = 99\%$ .

**[0073]** The term "specificity" refers to the number of false positives: i.e. if on 100 strains detected, 2 seem to belong to organisms for which the test is not designed, the specificity of the test is  $(100-2/100)\% = 98\%$ .

50 **[0074]** The probes selected as being "preferential" show a sensitivity and specificity of more than 80%, preferably more than 90% and most preferably more than 95%.

**[0075]** The term "primer" refers to a single stranded DNA oligonucleotide sequence capable of acting as a point of initiation for synthesis of a primer extension product which is complementary to the nucleic acid strand to be copied. The length and the sequence of the primer must be such that they allow to prime the synthesis of the extension products. Preferably the primer is about 5-50 nucleotides long. Specific length and sequence will depend on the complexity of the required DNA or RNA targets, as well as on the conditions of primer use such as temperature and ionic strength. The fact that amplification primers do not have to match exactly with the corresponding template sequence to warrant proper amplification is amply documented in the literature (Kwok et al., 1990).

[0076] The amplification method used can be either polymerase chain reaction (PCR; Saiki et al., 1988), ligase chain reaction (LCR; Landgren et al., 1988; Wu & Wallace, 1989; Barany, 1991), nucleic acid sequence-based amplification (NASBA; Guatelli et al., 1990; Compton, 1991), transcription-based amplification system (TAS; Kwoh et al., 1989), strand displacement amplification (SDA; Duck, 1990; Walker et al., 1992) or amplification by means of QB replicase (Lizardi et al., 1988; Lomeli et al., 1989) or any other suitable method to amplify nucleic acid molecules known in the art.

[0077] The oligonucleotides used as primers or probes may also comprise nucleotide analogues such as phosphorothioates (Matsukura et al., 1987), alkylphosphorothioates (Miller et al., 1979) or peptide nucleic acids (Nielsen et al., 1991; Nielsen et al., 1993) or may contain intercalating agents (Asseline et al., 1984).

[0078] As most other variations or modifications introduced into the original DNA sequences of the invention these variations will necessitate adaptations with respect to the conditions under which the oligonucleotide should be used to obtain the required specificity and sensitivity. However the eventual results of hybridisation will be essentially the same as those obtained with the unmodified oligonucleotides.

[0079] The introduction of these modifications may be advantageous in order to positively influence characteristics such as hybridization kinetics, reversibility of the hybrid-formation, biological stability of the oligonucleotide molecules, etc.

[0080] The term "solid support" can refer to any substrate to which an oligonucleotide probe can be coupled, provided that it retains its hybridization characteristics and provided that the background level of hybridization remains low. Usually the solid substrate will be a microtiter plate, a membrane (e.g. nylon or nitrocellulose) or a microsphere (bead). Prior to application to the membrane or fixation it may be convenient to modify the nucleic acid probe in order to facilitate fixation or improve the hybridization efficiency. Such modifications may encompass homopolymer tailing, coupling with different reactive groups such as aliphatic groups, NH<sub>2</sub> groups, SH groups, carboxylic groups, or coupling with biotin, haptens or proteins.

[0081] The term "labelled" refers to the use of labelled nucleic acids. Labelling may be carried out by the use of labelled nucleotides incorporated during the polymerase step of the amplification such as illustrated by Saiki et al. (1988) or Bej et al. (1990) or by the use of labelled primers, or by any other method known to the person skilled in the art. The nature of the label may be isotopic (<sup>32</sup>P, <sup>35</sup>S, etc.) or non-isotopic (biotin, digoxigenin, etc.).

[0082] The "sample" may be any biological material taken either directly from the infected human being (or animal), or after culturing (enrichment), or a sample taken from food or feed. Biological material may be e.g. expectorations of any kind, broncheolavages, blood, skin tissue, biopsies, lymphocyte blood culture material, colonies, etc. Said samples may be prepared or extracted according to any of the techniques known in the art.

[0083] The "target" material in these samples may be either genomic DNA or precursor RNA of the organism to be detected (= target organism), or amplified versions thereof as set out above. More specifically, the nucleic acid sequence of the target material is localized in the spacer region of the target organism(s).

[0084] Detection and identification of the target material can be performed by using one of the many electrophoresis methods, hybridization methods or sequencing methods described in literature and currently known by men skilled in the art. However, a very convenient and advantageous technique for the simultaneous detection of nucleic acids possibly present in biological samples is the Line Probe Assay technique. The Line Probe Assay (LiPA) is a reverse hybridization format (Saiki et al., 1989) using membrane strips onto which several oligonucleotide probes (including negative or positive control oligonucleotides) can be conveniently applied as parallel lines.

[0085] The LiPA technique, as described by Stuyver et al. (1993) and in international application WO 94/12670, provides a very rapid and user-friendly hybridization test. Results can be read within 4 h. after the start of the amplification. After amplification during which usually a non-isotopic label is incorporated in the amplified product, and alkaline denaturation, the amplified product is contacted with the probes on the membrane and the hybridization is carried out for about 1 to 1.5 h. Consequently, the hybrids formed are detected by an enzymatic procedure resulting in a visual purple-brown precipitate. The LiPA format is completely compatible with commercially available scanning devices, thus rendering automatic interpretation of the results possible. All those advantages make the LiPA format liable for use in a routine setting.

[0086] The LiPA format is not only an advantageous tool for identification and detection of pathogens at the species level but also at higher or lower taxonomical levels. For instance, probe-configurations on LiPA strips can be selected in such a manner that they can detect a complete genus (e.g. *Neisseria*, *Listeria*, etc.) or can identify subgroups within a genus (e.g. subgroups in the *Mycobacterium avium-intracellulare-scrofulaceum* complex) or can in some cases even detect subtypes (subspecies, serovars, sequevars, biovars, etc. whatever is clinically relevant) within a species.

[0087] It should be stressed that the ability to simultaneously generate hybridization results with a number of probes is an outstanding benefit of the LiPA technology. In many cases the amount of information which can be obtained by a particular combination of probes greatly outnumbers the data obtained by using single probe assays. Therefor the selection of probes on the membrane strip is of utmost importance since an optimized set of probes will generate the maximum of information possible. This is more particularly exemplified further herein.

[0088] The fact that different probes can be combined on one strip also offers the possibility to conveniently cope

with a lack of sensitivity due to sequence heterogeneity in the target region of the group of organisms to be detected. Due to this heterogeneity, two or more probes may be required to positively identify all organisms of the particular group. These probes can be applied to membrane strips at different locations and the result is interpreted as positive if at least one of these probes is positive. Alternatively these probes can be applied as a mixture at the same location, hereby reducing the number of lines on a strip. This reduction may be convenient in order to make the strip more concise or to be able to extend the total number of probes on one strip. Another alternative approach, in view of its practical benefits, is the synthesis of oligonucleotides harbouring the sequences of two (or more) different probes (=degenerate probes) which then can be further processed and applied to the strip as one oligonucleotide molecule. This approach would considerably simplify the manufacturing procedures of the LiPA-strips. For example, probes with nucleotide sequences A and B are both required to detect all strains of taxon X. In the latter alternative a probe can be synthesized having the nucleotide sequence AB. This probe will have the combined characteristics of probes A and B.

**[0089]** By virtue of the above-mentioned properties the LiPA system can be considered as a preferential format for a hybridization method wherein several organisms need to be detected simultaneously in a sample. Moreover, as described in the examples section, the LiPA system is a preferred format for a selection method for the experimental evaluation and selection of theoretically designed probes.

**[0090]** However, it should be clear that any other hybridization assay, whereby different probes are used under the same hybridization and wash conditions can be used for the above-mentioned detection and/or selection methods. For example, it may be possible to immobilize the target nucleic acid to a solid support, and use mixtures of different probes, all differently labeled, resulting in a different detection signal for each of the probes hybridized to the target.

**[0091]** As an example, the procedure to be followed for the detection of one or more organisms in a sample using the LiPA format is outlined below :

- First, the nucleic acids of the organism(s) to be detected in the sample, is made available for amplification and/or hybridization.
- Secondly, the nucleic acids, if present, are amplified with one or another target amplification system, as specified below. Usually, amplification is needed to enhance the subsequent hybridization signal. However for some samples or some organisms amplification might not be necessary. This might also be the case if, for the detection of the hybrids formed, highly sensitive signal-amplification systems are used.
- Thirdly, eventually after a denaturation step, the nucleic acids present in the sample or the resulting amplified product are contacted with LiPA strips onto which one or more DNA-probes, allowing the detection of the organisms of interest, are immobilized, and hybridization is allowed to proceed.
- Finally, eventually after having performed a wash step, the hybrids are detected using a convenient and compatible detection system. From the hybridization signals or patterns observed the presence or absence of one or several organisms screened for in that particular biological sample can be deduced.

**[0092]** The amplification system used may be more or less universal, depending on the specific application needed.

**[0093]** By using universal primers located in the conserved flanking regions (16S and 23S gene) of the rRNA spacer, the spacer region of most if not all organisms of eubacterial origin will be amplified. The same result may be obtained by using a combination of different sets of primers with reduced universality (multiplex amplification, i.e. an amplification procedure in which two or more primer sets are used simultaneously in one and the same reaction mixture).

**[0094]** For some applications it may be appropriate to amplify not all organisms present in the sample but more specifically, beforehand defined taxa. This may be achieved using specific primers located either in less conserved parts of the flanking genes of the spacers (e.g. MYCP1-5 for amplification of the spacer region of mycobacteria) or located in the spacers themselves (e.g. LIS-P1-P7, BRU-P1-4, CHTR-P1-2 and YEC-P1-2 for specific amplification of the spacer region(s) of Listeria species, Brucella species, Chlamydia trachomatis, and Yersinia enterocolitica respectively).

**[0095]** The present invention thus provides a method for detection and identification of at least one micro-organism, or for the simultaneous detection of several micro-organisms in a sample, comprising the steps of:

- (i) if need be releasing, isolating and/or concentrating the polynucleic acids from the micro-organism(s) to be detected in the sample;
- (ii) if need be amplifying the 16S-23S rRNA spacer region, or a part of it, from the micro-organism(s) to be detected, with at least one suitable primer pair;
- (iii) hybridizing the polynucleic acids of step (i) or (ii) with a set of probes comprising at least two probes, under the same hybridization and wash conditions, with said probes being selected from the sequences of table 1a or equivalents thereof and/or from taxon-specific probes derived from any of the spacer sequences represented in figs. 1-103, with said taxon-specific probe being selected such that it is capable of hybridizing under the same

hybridization and wash conditions as at least one of the probes of table 1a;

(iv) detecting the hybrids formed in step (iii);

(v) identification of the micro-organism(s) present in the sample from the differential hybridization signals obtained in step (iv).

[0096] The probes as mentioned in table 1a are all selected in such a way that they show the desired hybridization characteristics at a hybridization and wash temperature of 50°C in a preferred hybridization and wash medium of 3X SSC and 20% formamide.

[0097] The term "equivalents" of a probe, also called "variants" or "homologues" or "obvious derivatives", refers to probes differing in sequence from any of the probes specified in table 1 either by addition to or removal from any of their respective extremities of one or several nucleotides, or by changing one or more nucleotides within said sequences, or a combination of both, provided that said equivalents still hybridize with the same RNA or DNA target as the corresponding unmodified probe sequence. Said equivalents share at least 75% homology, preferably more than 80%, most preferably more than 85% homology with the corresponding unmodified probe sequence. It should be noted that, when using an equivalent of a probe, it may be necessary to modify the hybridization conditions to obtain the same specificity as the corresponding unmodified probe. As a consequence, since it is the aim of this invention to use a set of probes which work under the same hybridization and wash conditions, it will also be necessary to modify accordingly the sequence of the other probes, belonging to the same set as the original unmodified probe. These modifications can be done according to principles known in the art, e.g. such as those described in Hames B and Higgins S (Eds): Nucleic acid hybridization. Practical approach. IRL Press, Oxford, UK, 1985.

[0098] The invention also provides for a method to select taxon-specific probes from the spacer region sequence(s) of said taxon, said probes being selected such that they show their desired hybridization characteristics under unified hybridization and wash conditions.

[0099] The term "unified" conditions means that these conditions are the same for the different probes enabling the detection of different taxa.

[0100] Preferentially, the present invention provides for a method as described above wherein at least 2 micro-organisms are detected simultaneously.

[0101] In a preferred embodiment, the set of probes as described in step (iii) is comprising at least two probes being selected from the sequences of table 1a, or equivalents thereof.

[0102] In another embodiment, the set of probes as described in step (iii) is comprising at least one probe being selected from the sequences of table 1a, or equivalents thereof, and at least one taxon-specific probe derived from any of the spacer sequences as represented in figs. 1-103.

[0103] In still another embodiment, the set of probes as described in step (iii) is comprising at least two taxon-specific probes derived from any of the spacer sequences as represented in figs. 1-103.

[0104] The present invention also provides for a method as described above, wherein the probes as specified in step (iii) are combined with at least one other probe, preferentially also from the 16S-23S rRNA spacer region, enabling the simultaneous detection of different pathogenic bacteria liable to be present in the same sample.

[0105] The organisms of clinical relevance present in biological samples may vary considerably depending on the origin of the sample. The most common pathogenic bacteria which may be found in sputum samples, or in samples originating from the respiratory tract, are :

- Moraxella catarrhalis
- Streptococcus pneumoniae
- Haemophilus influenzae
- Pseudomonas aeruginosa
- Mycoplasma pneumoniae
- Acinetobacter species
- Mycobacterium species
- Staphylococcus aureus
- Legionella pneumophila

[0106] A LiPA-strip harbouring spacer-probes enabling the detection of most if not all of these organisms would be extremely beneficial for reasons explained above.

[0107] Evidently, this also applies for other biological samples, as there are :

cerebrospinal fluid, urogenital samples, gastrointestinal samples, blood, urine, food products, soil, etc. For example, a preferred panel for cerebrospinal fluid would contain probe combinations enabling the detection and differentiation of the following organisms :

- Neisseria meningitidis
- Streptococcus pneumoniae
- Streptococcus agalactiae
- Listeria monocytogenes
- 5 - Mycobacterium tuberculosis

[0108] For some of the above mentioned organisms, spacer probes were already designed in a previous patent application (WO 91/16454). In order to be able to detect most pathogens possibly present in a sample in a single test, the probes of the present invention may be combined with at least one of the probes of WO 91/16454, or their obvious derivatives as specified in WO 91/16454. For clarity, these probes are listed hereafter:

Neisseria gonorrhoeae: NGI1: CGATGCGTCGTTATTCTACTTCGC  
 15 NGI2: TTCGTTTACCTACCCGTTGACTAAGTAAGCAAAC

Neisseria meningitidis: NMI1: GGTCAAGTGTGACGTCGCCCTG  
 20 NMI2: GTTCTTGGTCAAGTGTGACGTC  
 NMI3: GCGTTCGTTATAGCTATCTACTGTGC  
 NMI4: TCGGTTTCGATATTGCTATCTACTGTGCA  
 25 NMI5: TTTTGTTCCTTGGTCAAGTGTGACGTCGCCCTGAA  
 TGGATTCTGTTCCATT  
 NMI6: TTTGCCTAACATTCCGTTGACTAGAACATCAGAC

30 Haemophilus ducreyi HDI1: TTATTATGCGCGAGGCATATTG  
Branhamella catharralis BCI1: TTAAACATCTTACCAAAG  
 BCI2: TTGATGTTTAAACTTGCTTGGTGGGA  
 35 Bordetella pertussis BPI1: CCACACCCATCCTCTGGACAGGCTT  
Haemophilus influenzae HII1: ACGCATCAAATTGACCGCACTT  
 HII2: ACTTTGAAGTGAAAACCTTAAAG  
 40 Streptococcus agalactiae SAI1: AATCGAAAGGTTCAAATTGTT  
 SAI2: GGAAACCTGCCATTTGCGTCTT  
 SAI3: TCCACGATCTAGAAATAGATTGTAGAA  
 45 SAI4: TCTAGTTTTAAAGAACTAGGTT  
Streptococcus pneumoniae SPI1: GTGAGAGATCACCAAGTAATGCA  
 SPI2: AGGAACTGCGCATTGGTCTT  
 50 SPI3: GAGTTTATGACTGAAAGGTCAGAA

[0109] The invention thus provides for a method as described above, wherein said sample is originating from the respiratory tract, and wherein the set of probes as defined in step (iii) comprises at least one probe chosen from the following spacer probes:

EP 1 088 899 A2

	MYC-ICG-1 :	ACTGGATAGTGGTTGCGAGCATCTA	(SEQ ID NO 1)
	MYC-ICG-22 :	CTTCTGAATAGTGGTTGCGAGCATCT	(SEQ ID NO 2)
5	MTB-ICG-1 :	GGGTGCATGACAACAAAGTTGGCCA	(SEQ ID NO 3)
	MTB-ICG-2 :	GACTTGTTCCAGGTGTTGTCCCAC	(SEQ ID NO 4)
	MTB-ICG-3 :	CGGCTAGCGGTGGCGTGTTCT	(SEQ ID NO 5)
10	MAI-ICG-1 :	CAACAGCAAATGATTGCCAGACACAC	(SEQ ID NO 6)
	MIL-ICG-11 :	GAGGGGTTCCCGTCTGTAGTG	(SEQ ID NO 7)
	MIL-ICG-22 :	TGAGGGGTTCTCGTCTGTAGTG	(SEQ ID NO 8)
15	MAC-ICG-1 :	CACTCGGTCGATCCGTGTGGA	(SEQ ID NO 9)
	MAV-ICG-1 :	TCGGTCCGTCCGTGTGGAGTC	(SEQ ID NO 10)

20

25

30

35

40

45

50

55

	MAV-ICG-22 :	GTGGCCGGCGTTCATCGAAA	(SEQ ID NO 11)
	MIN-ICG-1 :	GCATAGTCCTTAGGGCTGATGCGTT	(SEQ ID NO 12)
5	MIN-ICG-2 :	GCTGATGCGTTCGTCGAAATGTGTA	(SEQ ID NO 13)
	MIN-ICG-22 :	CTGATGCGTTCGTCGAAATGTGT	(SEQ ID NO 14)
	MIN-ICG-222 :	TGATGCGTTCGTCGAAATGTGT	(SEQ ID NO 15)
10	MIN-ICG-2222 :	GGCTGATGCGTTCGTCGAAATGTGTAA	(SEQ ID NO 16)
	MAL-ICG-1 :	ACTAGATGAACGCGTAGTCCTTGT	(SEQ ID NO 17)
	MHEF-ICG-1 :	TGGACGAAAACCGGGTGCACAA	(SEQ ID NO 18)
15	MAH-ICG-1 :	GTGTAATTTCTTTTTTA	(SEQ ID NO 19)
		ACTCTTGTGTGTAAGTAAGTG	(SEQ ID NO 20)
	MCO-ICG-11 :	TGGCCGGCGTGTTCATCGAAA	(SEQ ID NO 21)
20	MTH-ICG-11 :	GCACTTCAATTGGTGAAGTGCGAGCC	(SEQ ID NO 22)
	MTH-ICG-2 :	GCGTGGTCTTCATGGCCGG	(SEQ ID NO 23)
	MEF-ICG-11 :	ACGCGTGGTCCCTCGTGG	(SEQ ID NO 24)
25	MSC-ICG-1 :	TCGGCTCGTTCTGAGTGGTGTC	(SEQ ID NO 25)
	MKA-ICG-1 :	GATGCGTTTGCTACGGGTAGCGT	(SEQ ID NO 26)
	MKA-ICG-2 :	GATGCGTTGCCTACGGGTAGCGT	(SEQ ID NO 27)
30	MKA-ICG-3 :	ATGCGTTGCCCTACGGGTAGCGT	(SEQ ID NO 28)
	MKA-ICG-4 :	CGGGCTCTGTTGAGAGTTGTC	(SEQ ID NO 182)
	MKA-ICG-5 :	CCCTCAGGGATTTTCTGGGTGTTG	(SEQ ID NO 183)
35	MKA-ICG-6 :	GGACTCGTCCAAGAGTGTGTCC	(SEQ ID NO 184)
	MKA-ICG-7 :	TCGGGCTTGCCAGAGCTGTT	(SEQ ID NO 185)
	MKA-ICG-8 :	GGGTGCGCAACAGCAAGCGA	(SEQ ID NO 186)
40	MKA-ICG-9 :	GATGCGTTGCCCCACGGG	(SEQ ID NO 187)
	MKA-ICG-10 :	CCCTACGGGTAGCGTGTCTTTTG	(SEQ ID NO 29)
	MCH-ICG-1 :	GGTGTGGACTTTGACTTCTGAATAG	(SEQ ID NO 30)
45	MCH-ICG-2 :	CGGCAAAACGTCGGACTGTCA	(SEQ ID NO 210)
	MCH-ICG-3 :	GGTGTGGTCTTGACTTATGGATAG	(SEQ ID NO 31)
	MGO-ICG-1 :	AACACCCTCGGGTGCTGTCC	(SEQ ID NO 32)
50	MGO-ICG-2 :	GTATGCGTTGTCGTTGCGGGC	(SEQ ID NO 33)
	MGO-ICG-5 :	CGTGAGGGGTCATCGTCTGTAG	(SEQ ID NO 175)
55	MUL-ICG-1 :	GGTTTCGGGATGTTGTCCCACC	(SEQ ID NO 176)
	MGV-ICG-1 :	CGACTGAGGTGACGTGGTGT	



	MGV-ICG-2 :	GGTGTGTTGAGCATTGAATAGTGGTTGC	(SEQ ID NO 177)
	MGV-ICG-3 :	TCGGGCCGCGTGTTTCGTCAAA	(SEQ ID NO 211)
5	MXE-ICG-1 :	GTTGGGCAGCAGGCAGTAACC	(SEQ ID NO 178)
	MSI-ICG-1 :	CCGGCAACGGTTACGTGTTC	(SEQ ID NO 179)
	MFO-ICG-1 :	TCGTTGGATGGCCTCGCACCT	(SEQ ID NO 180)
10	MFO-ICG-2 :	ACTTGGCGTGGGATGCGGGAA	(SEQ ID NO 181)
	MML-ICG-1 :	CGGATCGATTGAGTGCTTGTCCC	(SEQ ID NO 188)
	MML-ICG-2 :	TCTAAATGAACGCACTGCCGATGG	(SEQ ID NO 189)
15	MCE-ICG-1 :	TGAGGGAGCCCGTGCCTGTA	(SEQ ID NO 190)
	MHP-ICG-1 :	CATGTTGGGCTTGATCGGGTGC	(SEQ ID NO 191)
20	PA-ICG 1 :	TGGTGTGCTGCGTGATCCGAT	(SEQ ID NO 34)
	PA-ICG 2 :	TGAATGTTCTGTGGATGAACATTGATT	(SEQ ID NO 35)
	PA-ICG 3 :	CACTGGTGATCATTCAAGTCAAG	(SEQ ID NO 36)
25	PA-ICG 4 :	TGAATGTTCTGT(G/A)(G/A)ATGAACATTGATTTCTGGTC	(SEQ ID NO 37)
	PA-ICG 5 :	CTCTTTCACCTGGTGATCATTCAAGTCAAG	(SEQ ID NO 38)
30	MPN-ICG 1 :	ATCGGTGGTAAATTAAACCCAAATCCCTGT	(SEQ ID NO 49)
	MPN-ICG 2 :	CAGTTCTGAAAGAACATTTCCGCTTCTTTC	(SEQ ID NO 50)
	MGE-ICG 1 :	CACCCATTAATTTTTTTCGGTGTTAAACCC	(SEQ ID NO 51)
35	Mycoplasma-ICG :	CAAACTGAAAACGACAATCTTTCTAGTTCC	(SEQ ID NO 52)
	STAU-ICG 1 :	TACCAAGCAAACCGAGTGAATAAAGAGTT	(SEQ ID NO 53)
	STAU-ICG 2 :	CAGAAGATGCGGAATAACGTGAC	(SEQ ID NO 54)
40	STAU-ICG 3 :	AACGAAGCCGTATGTGAGCATTTGAC	(SEQ ID NO 55)
	STAU-ICG 4 :	GAACGTAACTTCATGTTAACGTTTGACTTAT	(SEQ ID NO 56)
	ACI-ICG 1 :	GCTTAAGTGCACAGTGCTCTAAACTGA	(SEQ ID NO 57)
45	ACI-ICG 2 :	CACGGTAATTAGTGTGATCTGACGAAG	(SEQ ID NO 58)

and more preferably from the following spacer probes:

50

55

	MYC-ICG-1 :	ACTGGATAGTGGTTGCGAGCATCTA	(SEQ ID NO 1)
5	MYC-ICG-22 :	CTTCTGAATAGTGGTTGCGAGCATCT	(SEQ ID NO 2)
	MTB-ICG-1 :	GGGTGCATGACAACAAAGTTGGCCA	(SEQ ID NO 3)
	MTB-ICG-2 :	GACTTGTTCCAGGTGTTGTCCCAC	(SEQ ID NO 4)
10	MTB-ICG-3 :	CGGCTAGCGGTGGCGTGTCT	(SEQ ID NO 5)
	MAI-ICG-1 :	CAACAGCAAATGATTGCCAGACACAC	(SEQ ID NO 6)
15			
20			
25			
30			
35			
40			
45			
50			
55			

	MIL-ICG-11 :	GAGGGGTTCCCGTCTGTAGTG	(SEQ ID NO 7)
	MIL-ICG-22 :	TGAGGGGTTCTCGTCTGTAGTG	(SEQ ID NO 8)
5	MAC-ICG-1 :	CACTCGGTCGATCCGTGTGGA	(SEQ ID NO 9)
	MAV-ICG-1 :	TCGGTCCGTCCGTGTGGAGTC	(SEQ ID NO 10)
	MAV-ICG-22 :	GTGGCCGGCGTTCATCGAAA	(SEQ ID NO 11)
10	MIN-ICG-1 :	GCATAGTCCTTAGGGCTGATGCGTT	(SEQ ID NO 12)
	MAL-ICG-1 :	ACTAGATGAACGCGTAGTCCTTGT	(SEQ ID NO 17)
	MCO-ICG-11 :	TGGCCGGCGTGTTCATCGAAA	(SEQ ID NO 20)
15	MTH-ICG-11 :	GCACTTCAATTGGTGAAGTGCGAGCC	(SEQ ID NO 21)
	MTH-ICG-2 :	GCGTGGTCTTCATGGCCGG	(SEQ ID NO 22)
	MEF-ICG-11 :	ACGCGTGGTCCCTTCGTGG	(SEQ ID NO 23)
20	MSC-ICG-1 :	TCGGCTCGTTCTGAGTGGTGTC	(SEQ ID NO 24)
	MKA-ICG-3 :	ATGCGTTGCCCTACGGGTAGCGT	(SEQ ID NO 27)
	MKA-ICG-4 :	CGGGCTCTGTTCGAGAGTTGTC	(SEQ ID NO 28)
25	MKA-ICG-5 :	CCCTCAGGGATTTTCTGGGTGTTG	(SEQ ID NO 182)
	MKA-ICG-6 :	GGACTCGTCCAAGAGTGTGTCC	(SEQ ID NO 183)
	MKA-ICG-7 :	TCGGGCTTGCCAGAGCTGTT	(SEQ ID NO 184)
30	MKA-ICG-8 :	GGGTGCGCAACAGCAAGCGA	(SEQ ID NO 185)
	MKA-ICG-9 :	GATGCGTTGCCCCCTACGGG	(SEQ ID NO 186)
	MKA-ICG-10 :	CCCTACGGGTAGCGTGTCTTTTG	(SEQ ID NO 187)
35	MCH-ICG-1 :	GGTGTGGACTTTGACTTCTGAATAG	(SEQ ID NO 29)
	MCH-ICG-2 :	CGGCAAAACGTCGGACTGTCA	(SEQ ID NO 30)
	MCH-ICG-3 :	GGTGTGGTCCTTGACTTATGGATAG	(SEQ ID NO 210)
40	MGO-ICG-5 :	CGTGAGGGGTCATCGTCTGTAG	(SEQ ID NO 33)
	MUL-ICG-1 :	GGTTTCGGGATGTTGTCCCACC	(SEQ ID NO 175)
	MGV-ICG-1 :	CGACTGAGGTCGACGTGGTGT	(SEQ ID NO 176)
45	MGV-ICG-2 :	GGTGTTTGAGCATTGAATAGTGGTTGC	(SEQ ID NO 177)
	MGV-ICG-3 :	TCGGGCCGCGTGTTCGTCAA	(SEQ ID NO 211)
	MXE-ICG-1 :	GTTGGGCAGCAGGCAGTAACC	(SEQ ID NO 178)
50	MSI-ICG-1 :	CCGGCAACGGTTACGTGTTC	(SEQ ID NO 179)
	MFO-ICG-1 :	TCGTTGGATGGCCTCGCACCT	(SEQ ID NO 180)
	MFO-ICG-2 :	ACTTGGCGTGGGATGCGGGAA	(SEQ ID NO 181)
55	MML-ICG-1 :	CGGATCGATTGAGTGCTTGTCCC	(SEQ ID NO 188)

	MML-ICG-2 :	TCTAAATGAACGCACTGCCGATGG	(SEQ ID NO 189)
	MCE-ICG-1 :	TGAGGGAGCCCGTGCCTGTA	(SEQ ID NO 190)
5	MHP-ICG-1 :	CATGTTGGGCTTGATCGGGTGC	(SEQ ID NO 191)
	PA-ICG 1 :	TGGTGTGCTGCGTGATCCGAT	(SEQ ID NO 34)
10	PA-ICG 4 :	TGAATGTTTCGT(G/A)(G/A)ATGAACATTGATTTCTGGTC	(SEQ ID NO 37)
	PA-ICG 5 :	CTCTTTCACCTGGTGATCATTCAAGTCAAG	(SEQ ID NO 38)
15	MPN-ICG 1 :	ATCGGTGGTAAATTAAACCCAAATCCCTGT	(SEQ ID NO 49)
	MPN-ICG 2 :	CAGTTCTGAAAGAACATTTCCGCTTCTTTC	(SEQ ID NO 50)
20	MGE-ICG 1 :	CACCCATTAATTTTTTCGGTGTTAAACCC	(SEQ ID NO 51)
	Mycoplasma-ICG :	CAAACTGAAAACGACAATCTTTCTAGTTCC	(SEQ ID NO 52)
	STAU-ICG 1 :	TACCAAGCAAAACCGAGTGAATAAAGAGTT	(SEQ ID NO 53)
25	STAU-ICG 2 :	CAGAAGATGCCGAATAACGTGAC	(SEQ ID NO 54)
	STAU-ICG 3 :	AACGAAGCCGTATGTGAGCATTTGAC	(SEQ ID NO 55)
	STAU-ICG 4 :	GAACGTAAC TTCATGTTAACGTTTGACTTAT	(SEQ ID NO 56)
30	ACI-ICG 1 :	GCTTAAGTGCACAGTGCTCTAACTGA	(SEQ ID NO 57)
	ACI-ICG 2 :	CACGGTAATTAGTGTGATCTGACGAAG	(SEQ ID NO 58)

or equivalents of said probes,

35 and/or wherein the set of probes comprises at least one taxon-specific probe derived from the spacer region sequence corresponding to one of the micro-organisms to be detected in said sample, said spacer region sequence being chosen from any of the sequences as represented by SEQ ID NO 76 to 106, 157 to 174, 124, 125, 111 to 115, 139 to 144, or 126 to 130,

40 and with said probes or equivalents being possibly used in combination with any probe detecting at least one of the following organisms: Haemophilus influenzae, Streptococcus pneumoniae, Moraxella catarrhalis or Bordetella pertussis.

[0110] The above mentioned probes of the invention are designed for the detection of Mycobacterium species (SEQ ID NO 1 to 33 and 175 to 191), of Pseudomonas aeruginosa (SEQ ID NO 34 to 38), of Mycoplasma species (SEQ ID NO 49 to 52), of Staphylococcus aureus (SEQ ID NO 53 to 56) and of Acinetobacter baumannii (SEQ ID NO 57 and 58).

45 [0111] Preferentially, at least two, three, four, five, six, seven, eight or more of said probes are used simultaneously.

[0112] The invention also relates to a method as described above, wherein said sample is a sample taken from the cerebrospinal fluid, and wherein the set of probes as described in step (iii) comprises at least one probe chosen from the following spacer probes:

50

55

MYC-ICG-1 : ACTGGATAGTGGTTGCGAGCATCTA (SEQ ID NO 1)  
 MYC-ICG-22 : CTTCTGAATAGTGGTTGCGAGCATCT (SEQ ID NO 2)  
 5 MTB-ICG-1 : GGGTGCATGACAACAAAGTTGGCCA (SEQ ID NO 3)  
 MTB-ICG-2 : GACTTGTTCCAGGTGTTGTCCCAC (SEQ ID NO 4)  
 MTB-ICG-3 : CGGCTAGCGGTGGCGTGTCT (SEQ ID NO 5)  
 10 LIS-ICG 1 : CAAGTAACCGAGAATCATCTGAAAGTGAATC (SEQ ID NO 39)  
 LMO-ICG 1 : AAACAACCTTTACTTCGTAGAAGTAAATTGGTTAAG (SEQ ID NO 40)  
 15 LMO-ICG 2 : TGAGAGGTTAGTACTTCTCAGTATGTTTGTTTC (SEQ ID NO 41)  
 LMO-ICG 3 : AGGCACTATGCTTGAAGCATCGC (SEQ ID NO 42)  
 20 LISP-ICG 1 : CGTTTTTCATAAGCGATCGCACGTT (SEQ ID NO 212)

and preferably from the following spacer probes:

25 MYC-ICG-1 : ACTGGATAGTGGTTGCGAGCATCTA (SEQ ID NO 1)  
 MYC-ICG-22 : CTTCTGAATAGTGGTTGCGAGCATCT (SEQ ID NO 2)  
 MTB-ICG-1 : GGGTGCATGACAACAAAGTTGGCCA (SEQ ID NO 3)  
 30 MTB-ICG-2 : GACTTGTTCCAGGTGTTGTCCCAC (SEQ ID NO 4)  
 MTB-ICG-3 : CGGCTAGCGGTGGCGTGTCT (SEQ ID NO 5)  
 35 LIS-ICG 1 : CAAGTAACCGAGAATCATCTGAAAGTGAATC (SEQ ID NO 39)  
 LMO-ICG 3 : AGGCACTATGCTTGAAGCATCGC (SEQ ID NO 42)  
 40 LISP-ICG 1 : CGTTTTTCATAAGCGATCGCACGTT (SEQ ID NO 212)

or equivalents of said probes,

and/or wherein the set of probes comprises at least one taxon-specific probe derived from the spacer region sequence corresponding to one of the micro-organisms to be detected in said sample, said spacer region sequence being chosen from any of the sequences as represented by SEQ ID NO 116, 118-121, or 213-215,

and with said probes or equivalents being possibly used in combination with any probe detecting at least one of the following organisms: Neisseria meningitidis, Haemophilus influenzae or Streptococcus pneumoniae.

[0113] The above mentioned probes of the invention are designed for the detection of Mycobacterium species, and more particularly Mycobacterium tuberculosis (SEQ ID NO 1 to 5), and of Listeria species, more particularly Listeria monocytogenes (SEQ ID NO 39 to 42).

[0114] Preferentially, at least two, three, four, five, six, seven, eight or more of said probes are used simultaneously.

[0115] The invention also relates to a method as described above, wherein said sample is a sample taken from the urogenital tract, and wherein the set of probes as described in step (iii) comprises at least one probe chosen from the following spacer probes:

CHTR-ICG 1 : GGAAGAAGCCTGAGAAGGTTTCTGAC (SEQ ID NO 45)  
 CHTR-ICG 2 : GCATTATATGTAAGAGCAAGCATTCTATTTCA (SEQ ID NO 46)  
 5 CHTR-ICG 3 : GAGTAGCGTGGTGAGGACGAGA (SEQ ID NO 47)  
 CHTR-ICG 4 : GAGTAGCGCGGTGAGGACGAGA (SEQ ID NO 201)  
 CHPS-ICG 1 : GGATAACTGTCTTAGGACGGTTTGAC (SEQ ID NO 48)  
 10 MGE-ICG 1 : CACCCATTAATTTTTTCGGTGTTAAAACCC (SEQ ID NO 51)  
 Mycoplasma-ICG : CAAAACTGAAAACGACAATCTTTCTAGTTCC (SEQ ID NO 52)

15 or equivalents of said probes,  
 and/or wherein the set of probes comprises at least one taxon-specific probe derived from the spacer region sequence  
 corresponding to one of the micro-organisms to be detected in said sample, said spacer region sequence being chosen  
 from any of the sequences as represented by SEQ ID NO 122, 123, 197, 124 or 125,  
 with said probes or equivalents being possibly used in combination with any probe detecting at least one of the following  
 20 organisms: Neisseria gonorrhoeae, Haemophilus ducreyi or Streptococcus agalactiae.  
 [0116] The above mentioned probes of the invention are designed for the detection of Chlamydia species (SEQ ID  
 NO 45 to 48 and 201) and of Mycoplasma species (SEQ ID NO 51 and 52).  
 [0117] Preferentially, at least two, three, four, five, six or seven of said probes are used simultaneously.  
 25 [0118] The invention also relates to a method as described above, wherein said sample is a sample taken from food,  
 and wherein the set of probes as defined in step (iii) comprises at least one probe chosen from the following spacer  
 probes:

LIS-ICG 1 : CAAGTAACCGAGAATCATCTGAAAGTGAATC (SEQ ID NO 39)  
 30 LMO-ICG 1 : AAACAACCTTTACTTCGTAGAAAGTAAATTGGTTAAG  
 (SEQ ID NO 40)  
 LMO-ICG 2 : TGAGAGGTTAGTACTTCTCAGTATGTTTGTTT (SEQ ID NO 41)  
 35

40

45

50

55

	LMO-ICG 3 :	AGGCACTATGCTTGAAGCATCGC	(SEQ ID NO 42)
	LIV-ICG 1 :	GTTAGCATAAATAGGTAAGTATTTATGACACAAGTAAC	
5			(SEQ ID NO 43)
	LSE-ICG 1 :	AGTTAGCATAAGTAGTGTAAGTATTTATGACACAAG	(SEQ ID NO 44)
	LISP-ICG 1 :	CGTTTTTCATAAGCGATCGCACGTT	(SEQ ID NO 212)
10	STAU-ICG 1 :	TACCAAGCAAAACCGAGTGAATAAAGAGTT	(SEQ ID NO 53)
	STAU-ICG 2 :	CAGAAGATGCGGAATAACGTGAC	(SEQ ID NO 54)
	STAU-ICG 3 :	AACGAAGCCGTATGTGAGCATTTGAC	(SEQ ID NO 55)
15	STAU-ICG 4 :	GAACGTAACTTCATGTTAACGTTTGACTTAT	(SEQ ID NO 56)
	BRU-ICG 1 :	CGTGCCGCCTTCGTTTCTCTTT	(SEQ ID NO 59)
20	BRU-ICG 2 :	TTCGCTTCGGGGTGGATCTGTG	(SEQ ID NO 60)
	BRU-ICG 3 :	GCGTAGTAGCGTTTGCGTCGG	(SEQ ID NO 193)
	BRU-ICG 4 :	CGCAAGAAGCTTGCTCAAGCC	(SEQ ID NO 194)
25	SALM-ICG 1 :	CAAACTGACTTACGAGTCACGTTTGAG	(SEQ ID NO 61)
	SALM-ICG 2 :	GATGTATGCTTCGTTATCCACGCC	(SEQ ID NO 62)
	STY-ICG 1 :	GGTCAAACCTCCAGGGACGCC	(SEQ ID NO 63)
30	SED-ICG 1 :	GCGGTAATGTGTGAAAGCGTTGCC	(SEQ ID NO 64)
	YEC-ICG 1 :	GGAAAAGGTACTGCACGTGACTG	(SEQ ID NO 198)
	YEC-ICG 2 :	GACAGCTGAACTTATCCCTCCG	(SEQ ID NO 199)
35	YEC-ICG 3 :	GCTACCTGTTGATGTAATGAGTCAC	(SEQ ID NO 200)

and preferably from the following spacer probes:

40

45

50

55

	LIS-ICG 1 :	CAAGTAACCGAGAATCATCTGAAAGTGAATC	(SEQ ID NO 39)
	LMO-ICG 3 :	AGGCACTATGCTTGAAGCATCGC	(SEQ ID NO 42)
5	LISP-ICG 1 :	CGTTTTTCATAAGCGATCGCACGTT	(SEQ ID NO 212)
	STAU-ICG 1 :	TACCAAGCAAAACCGAGTGAATAAAGAGTT	(SEQ ID NO 53)
	STAU-ICG 2 :	CAGAAGATGCGGAATAACGTGAC	(SEQ ID NO 54)
10	STAU-ICG 3 :	AACGAAGCCGTATGTGAGCATTGAC	(SEQ ID NO 55)
	STAU-ICG 4 :	GAACGTAACTTCATGTTAACGTTTGACTTAT	(SEQ ID NO 56)
	BRU-ICG 2 :	TTCGCTTCGGGGTGGATCTGTG	(SEQ ID NO 60)
15	BRU-ICG 3 :	GCGTAGTAGCGTTTTCGCTCGG	(SEQ ID NO 193)
	BRU-ICG 4 :	CGCAAGAAGCTTGCTCAAGCC	(SEQ ID NO 194)
20	SALM-ICG 1 :	CAAACTGACTTACGAGTCACGTTTGAG	(SEQ ID NO 61)
	YEC-ICG 1 :	GGAAAAGGTACTGCACGTGACTG	(SEQ ID NO 198)
25	YEC-ICG 2 :	GACAGCTGAACTTATCCCTCCG	(SEQ ID NO 199)
	YEC-ICG 3 :	GCTACCTGTTGATGTAATGAGTCAC	(SEQ ID NO 200)

or equivalents of said probes,

30 and/or wherein the set of probes comprises at least one taxon-specific probe derived from the spacer region sequence corresponding to one of the micro-organisms to be detected in said sample, said spacer region sequence being chosen from any of the sequences as represented by SEQ ID NO 116, 118 -121, 213-215, 139-144, 131, 132, 154, 133-138, 195 or 196,

35 with said probes or equivalents being possibly used in combination with any probe detecting strains of Campylobacter species.

[0119] The above mentioned probes of the invention are designed for the detection of Listeria species (SEQ ID NO 39 to 44), of Staphylococcus species (SEQ ID NO 53 to 56), of Brucella species (SEQ ID NO 59, 60, 193 and 194), of Salmonella species (SEQ ID NO 61 to 64) and of Yersinia enterocolitica (SEQ ID NO 198 to 200).

[0120] Preferentially, at least two, three, four, five, six, seven, eight or more of said probes are used simultaneously.

40 [0121] The invention also relates to a method as described above, wherein said sample is a sample taken from the gastrointestinal tract of a patient, and wherein the set of probes as defined in step (iii) comprises at least one probe chosen from the following spacer probes:

45	SALM-ICG 1 :	CAAACTGACTTACGAGTCACGTTTGAG	(SEQ ID NO 61)
	SALM-ICG 2 :	GATGTATGCTTCGTTATTCCACGCC	(SEQ ID NO 62)
	STY-ICG 1 :	GGTCAAACCTCCAGGGACGCC	(SEQ ID NO 63)
50	SED-ICG 1 :	GCGGTAATGTGTGAAAGCGTTGCC	(SEQ ID NO 64)
	YEC-ICG 1 :	GGAAAAGGTACTGCACGTGACTG	(SEQ ID NO 198)
	YEC-ICG 2 :	GACAGCTGAACTTATCCCTCCG	(SEQ ID NO 199)
55	YEC-ICG 3 :	GCTACCTGTTGATGTAATGAGTCAC	(SEQ ID NO 200)

and preferably from the following spacer probes:



SALM-ICG 1 : CAAAACTGACTTACGAGTCACGTTTGAG (SEQ ID NO 61)  
 YEC-ICG 1 : GGAAAAGGTACTGCACGTGACTG (SEQ ID NO 198)  
 5 YEC-ICG 2 : GACAGCTGAACTTATCCCTCCG (SEQ ID NO 199)  
 YEC-ICG 3 : GCTACCTGTTGATGTAATGAGTCAC (SEQ ID NO 200)

10 or equivalents of said probes,  
 and/or wherein the set of probes comprises at least one taxon-specific probe derived from the spacer region sequence  
 corresponding to one of the micro-organisms to be detected in said sample, said spacer region sequence being chosen  
 from any of the sequences as represented by SEQ ID NO 133-138 or 195-196,  
 with said probes or equivalents being possibly used in combination with any probe detecting Campylobacter species.

15 [0122] The above mentioned probes of the invention are designed to detect Salmonella species (SEQ ID NO 61 to  
 64) and Yersinia enterocolitica (SEQ ID NO 198 to 200).

[0123] Preferentially, at least two, three, four, five, six or seven of said probes are used simultaneously.

[0124] The invention also relates to the use of the selected probes or their equivalents for the detection of specific  
 bacterial taxa, said taxa being either a complete genus, or a subgroup within a genus, a species, or even a subtype  
 20 within a species.

[0125] The invention thus provides for a method as described above to detect and identify one or more strains of  
Mycobacterium species and subspecies in a sample, wherein step (iii) comprises hybridizing to at least one of the  
 following probes:

MYC-ICG-1 : ACTGGATAGTGGTTGCGAGCATCTA (SEQ ID NO 1)  
 MYC-ICG-22 : CTTCTGAATAGTGGTTGCGAGCATCT (SEQ ID NO 2)  
 5 MTB-ICG-1 : GGGTGCATGACAACAAAGTTGGCCA (SEQ ID NO 3)  
 MTB-ICG-2 : GACTTGTTCCAGGTGTTGTCCAC (SEQ ID NO 4)  
 MTB-ICG-3 : CGGCTAGCGGTGGCGTGTCT (SEQ ID NO 5)  
 10 MAI-ICG-1 : CAACAGCAAATGATTGCCAGACACAC (SEQ ID NO 6)  
 MIL-ICG-11 : GAGGGGTTCCTCGTCTGTAGTG (SEQ ID NO 7)  
 MIL-ICG-22 : TGAGGGGTTCCTCGTCTGTAGTG (SEQ ID NO 8)  
 15 MAC-ICG-1 : CACTCGGTCGATCCGTGTGGA (SEQ ID NO 9)  
 MAV-ICG-1 : TCGGTCCGTCCGTGTGGAGTC (SEQ ID NO 10)  
 20 MAV-ICG-22 : GTGGCCGGCGTTCATCGAAA (SEQ ID NO 11)  
 MIN-ICG-1 : GCATAGTCCTTAGGGCTGATGCGTT (SEQ ID NO 12)  
 MIN-ICG-2 : GCTGATGCGTTCGTCGAAATGTGTA (SEQ ID NO 13)  
 25 MIN-ICG-22 : CTGATGCGTTCGTCGAAATGTGT (SEQ ID NO 14)  
 MIN-ICG-222 : TGATGCGTTCGTCGAAATGTGT (SEQ ID NO 15)  
 MIN-ICG-2222 : GGCTGATGCGTTCGTCGAAATGTGTAA (SEQ ID NO 16)  
 30 MAL-ICG-1 : ACTAGATGAACGCGTAGTCCTTGT (SEQ ID NO 17)  
 MHEF-ICG-1 : TGGACGAAAACCGGGTGCACAA (SEQ ID NO 18)  
 MAH-ICG-1 : GTGTAATTTCTTTTTTAACTCTTGTGTGTAAGTAAGTG  
 35  
 40  
 45  
 50  
 55

		(SEQ ID NO 19)
	MCO-ICG-11 : TGGCCGGCGTGTTCATCGAAA	(SEQ ID NO 20)
5	MTH-ICG-11 : GCACTTCAATTGGTGAAGTGCGAGCC	(SEQ ID NO 21)
	MTH-ICG-2 : GCGTGGTCTTCATGGCCGG	(SEQ ID NO 22)
	MEF-ICG-11 : ACGCGTGGTCCTTCGTGG	(SEQ ID NO 23)
10	MSC-ICG-1 : TCGGCTCGTTCTGAGTGGTGTC	(SEQ ID NO 24)
	MKA-ICG-1 : GATGCGTTTGCTACGGGTAGCGT	(SEQ ID NO 25)
	MKA-ICG-2 : GATGCGTTGCCTACGGGTAGCGT	(SEQ ID NO 26)
15	MKA-ICG-3 : ATGCGTTGCCCTACGGGTAGCGT	(SEQ ID NO 27)
	MKA-ICG-4 : CGGGCTCTGTTGAGAGTTGTC	(SEQ ID NO 28)
	MKA-ICG-5 : CCCTCAGGGATTTTCTGGGTGTTG	(SEQ ID NO 182)
20	MKA-ICG-6 : GGA CT CGTCCAAGAGTGTTGTCC	(SEQ ID NO 183)
	MKA-ICG-7 : TCGGGCTTGGCCAGAGCTGTT	(SEQ ID NO 184)
	MKA-ICG-8 : GGGTGCGCAACAGCAAGCGA	(SEQ ID NO 185)
25	MKA-ICG-9 : GATGCGTTGCCCCTACGGG	(SEQ ID NO 186)
	MKA-ICG-10 : CCCTACGGGTAGCGTGTTCTTTTG	(SEQ ID NO 187)
30	MCH-ICG-1 : GGTGTGGACTTTGACTTCTGAATAG	(SEQ ID NO 29)
	MCH-ICG-2 : CGGCAAAACGTCGGACTGTCA	(SEQ ID NO 30)
	MGO-ICG-1 : AACACCCTCGGGTGCTGTCC	(SEQ ID NO 31)
35	MGO-ICG-2 : GTATGCGTTGTGTTGCGCGC	(SEQ ID NO 32)
	MGO-ICG-5 : CGTGAGGGGTCATCGTCTGTAG	(SEQ ID NO 33)
	MUL-ICG-1 : GGTTTCGGGATGTTGTCCCACC	(SEQ ID NO 175)
40	MGV-ICG-1 : CGACTGAGGTCGACGTGGTGT	(SEQ ID NO 176)
	MGV-ICG-2 : GGTGTTTGAGCATTGAATAGTGGTTGC	(SEQ ID NO 177)
	MXE-ICG-1 : GTTGGGCAGCAGGCAGTAACC	(SEQ ID NO 178)
45	MSI-ICG-1 : CCGGCAACGGTTACGTGTTT	(SEQ ID NO 179)
	MFO-ICG-1 : TCGTTGGATGGCCTCGCACCT	(SEQ ID NO 180)
	MFO-ICG-2 : ACTTGGCGTGGGATGCGGGAA	(SEQ ID NO 181)
50	MML-ICG-1 : CGGATCGATTGAGTGCTTGTCCT	(SEQ ID NO 188)
	MML-ICG-2 : TCTAAATGAACGCACTGCCGATGG	(SEQ ID NO 189)
	MCE-ICG-1 : TGAGGGAGCCCGTGCCTGTA	(SEQ ID NO 190)
55	MHP-ICG-1 : CATGTTGGGCTTGATCGGGTGC	(SEQ ID NO 191)

## EP 1 088 899 A2

and more preferably to at least one probe of the following restricted group of spacer probes:

5

10

15

20

25

30

35

40

45

50

55

	MYC-ICG-1 :	ACTGGATAGTGGTTGCGAGCATCTA	(SEQ ID NO 1)
	MYC-ICG-22 :	CTTCTGAATAGTGGTTGCGAGCATCT	(SEQ ID NO 2)
5	MTB-ICG-1 :	GGGTGCATGACAACAAAGTTGGCCA	(SEQ ID NO 3)
	MTB-ICG-2 :	GACTTGTTCCAGGTGTTGTCCAC	(SEQ ID NO 4)
	MTB-ICG-3 :	CGGCTAGCGGTGGCGTGTCT	(SEQ ID NO 5)
10	MAI-ICG-1 :	CAACAGCAAATGATTGCCAGACACAC	(SEQ ID NO 6)
	MIL-ICG-11 :	GAGGGGTTCCTCGTCTGTAGTG	(SEQ ID NO 7)
	MIL-ICG-22 :	TGAGGGGTTCCTCGTCTGTAGTG	(SEQ ID NO 8)
15	MAC-ICG-1 :	CACTCGGTCGATCCGTGTGGA	(SEQ ID NO 9)
	MAV-ICG-1 :	TCGGTCCGTCCGTGTGGAGTC	(SEQ ID NO 10)
	MAV-ICG-22 :	GTGGCCGGCGTTCATCGAAA	(SEQ ID NO 11)
20	MIN-ICG-1 :	GCATAGTCCTTAGGGCTGATGCGTT	(SEQ ID NO 12)
	MAL-ICG-1 :	ACTAGATGAACGCGTAGTCCTTGT	(SEQ ID NO 17)
	MCO-ICG-11 :	TGGCCGGCGTGTTCATCGAAA	(SEQ ID NO 20)
25	MTH-ICG-11 :	GCACTTCAATTGGTGAAGTGCGAGCC	(SEQ ID NO 21)
	MTH-ICG-2 :	GCGTGGTCTTCATGGCCGG	(SEQ ID NO 22)
	MEF-ICG-11 :	ACGCGTGGTCTTCGTGG	(SEQ ID NO 23)
30	MSC-ICG-1 :	TCGGCTCGTTCTGAGTGGTGTC	(SEQ ID NO 24)
	MKA-ICG-3 :	ATGCGTTGCCCTACGGGTAGCGT	(SEQ ID NO 27)
	MKA-ICG-4 :	CGGGCTCTGTTCGAGAGTTGTC	(SEQ ID NO 28)
35	MKA-ICG-5 :	CCCTCAGGGATTTTCTGGGTGTTG	(SEQ ID NO 182)
	MKA-ICG-6 :	GGA CTCGTCCAAGAGTGTGTCC	(SEQ ID NO 183)
	MKA-ICG-7 :	TCGGGCTTGGCCAGAGCTGTT	(SEQ ID NO 184)
40	MKA-ICG-8 :	GGGTGCGCAACAGCAAGCGA	(SEQ ID NO 185)
	MKA-ICG-9 :	GATGCGTTGCCCCTACGGG	(SEQ ID NO 186)
	MKA-ICG-10 :	CCCTACGGGTAGCGTGTCTTTTG	(SEQ ID NO 187)
45	MCH-ICG-1 :	GGTGTGGACTTTGACTTCTGAATAG	(SEQ ID NO 29)
	MCH-ICG-2 :	CGGCAAAACGTCGGACTGTCA	(SEQ ID NO 30)
	MCH-ICG-3 :	GGTGTGGTCCTTGACTTATGGATAG	(SEQ ID NO 210)
50	MGO-ICG-5 :	CGTGAGGGGTCATCGTCTGTAG	(SEQ ID NO 33)
	MUL-ICG-1 :	GGTTTCGGGATGTTGTCCACC	(SEQ ID NO 175)
	MGV-ICG-1 :	C GACTGAGGTCGACGTGGTGT	(SEQ ID NO 176)
55	MGV-ICG-2 :	GGTGTTTGAGCATTGAATAGTGGTTGC	(SEQ ID NO 177)

	MGV-ICG-3 :	TCGGGCCGCGTGTTCGTCAAA	(SEQ ID NO 211)
	MXE-ICG-1 :	GTTGGGCAGCAGGCAGTAACC	(SEQ ID NO 178)
5	MSI-ICG-1 :	CCGGCAACGGTTACGTGTTC	(SEQ ID NO 179)
	MFO-ICG-1 :	TCGTTGGATGGCCTCGCACCT	(SEQ ID NO 180)
	MFO-ICG-2 :	ACTTGGCGTGGGATGCGGGAA	(SEQ ID NO 181)
10	MML-ICG-1 :	CGGATCGATTGAGTGCTTGTC	(SEQ ID NO 188)
	MML-ICG-2 :	TCTAAATGAACGCACTGCCGATGG	(SEQ ID NO 189)
	MCE-ICG-1 :	TGAGGGAGCCCGTGCCTGTA	(SEQ ID NO 190)
15	MHP-ICG-1 :	CATGTTGGGCTTGATCGGGTGC	(SEQ ID NO 191)

or to equivalents of said probes,

20 and/or to any probe derived from SEQ ID NO 76-110, or 157-174 provided said probe hybridizes specifically to a Mycobacterium species.

[0126] The sequences represented by SEQ ID NO 76-110 and 157-174 are new.

[0127] Preferentially, at least two, three, four, five, six, seven, eight or more of said probes are used simultaneously.

25 [0128] As described above, the preferred restricted set of probes are those probes which showed a sensitivity and specificity of more than 80%, preferably more than 90%, most preferably more than 95%, under the specific hybridization conditions as described in the examples section.

[0129] In one specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium tuberculosis complex strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

30	MTB-ICG-1 :	GGGTGCATGACAACAAAGTTGGCCA	(SEQ ID NO 3)
	MTB-ICG-2 :	GACTTGTTCCAGGTGTTGTCCCAC	(SEQ ID NO 4)
35	MTB-ICG-3 :	CGGCTAGCGGTGGCGTGTCT	(SEQ ID NO 5)

or to equivalents of said probes,

40 and/or to any probe derived from SEQ ID NO 76 provided said probe hybridizes specifically to the M. tuberculosis complex. The M. tuberculosis complex comprises M. tuberculosis, M. bovis, M. bovis BCG, M. africanum and M. microti strains.

[0130] The sequence represented in SEQ ID NO 76 is new.

[0131] Preferentially, at least two, or three of said probes are used simultaneously.

45 [0132] In another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium strains from the MAIS-complex, wherein step (iii) comprises hybridizing to at least one of the following probes:

50

55

	MAI-ICG-1 :	CAACAGCAAATGATTGCCAGACACAC	(SEQ ID NO 6)
	MIL-ICG-11 :	GAGGGGTTCCTCGTCTGTAGTG	(SEQ ID NO 7)
5	MIL-ICG-22 :	TGAGGGGTTCCTCGTCTGTAGTG	(SEQ ID NO 8)
	MAC-ICG-1 :	CACTCGGTCGATCCGTGTGGA	(SEQ ID NO 9)
	MAV-ICG-1 :	TCGGTCCGTCCGTGTGGAGTC	(SEQ ID NO 10)
10	MAV-ICG-22 :	GTGGCCGGCGTTCATCGAAA	(SEQ ID NO 11)
	MIN-ICG-1 :	GCATAGTCCTTAGGGCTGATGCGTT	(SEQ ID NO 12)
	MIN-ICG-2 :	GCTGATGCGTTCGTCGAAATGTGTA	(SEQ ID NO 13)
15	MIN-ICG-22 :	CTGATGCGTTCGTCGAAATGTGT	(SEQ ID NO 14)
	MIN-ICG-222 :	TGATGCGTTCGTCGAAATGTGT	(SEQ ID NO 15)
20	MIN-ICG-2222 :	GGCTGATGCGTTCGTCGAAATGTGTAA	(SEQ ID NO 16)
	MAL-ICG-1 :	ACTAGATGAACGCGTAGTCCTTGT	(SEQ ID NO 17)
	MHEF-ICG-1 :	TGGACGAAAACCGGGTGCACAA	(SEQ ID NO 18)
25	MAH-ICG-1 :	GTGTAATTTCTTTTTTAACCTTGTGTGTAAGTAAGTG	(SEQ ID NO 19)
	MCO-ICG-11 :	TGGCCGGCGTGTTCATCGAAA	(SEQ ID NO 20)
30	MTH-ICG-11 :	GCACTTCAATTGGTGAAGTGCGAGCC	(SEQ ID NO 21)
	MTH-ICG-2 :	GCGTGGTCTTCATGGCCGG	(SEQ ID NO 22)
	MEF-ICG-11 :	ACGCGTGGTCCTTCGTGG	(SEQ ID NO 23)
35	MSC-ICG-1 :	TCGGCTCGTTCGTGAGTGGTGTC	(SEQ ID NO 24)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 77-100 or 108-110, provided said probe hybridizes specifically to strains from the MAIS complex. The MAIS complex as defined in this invention comprises all strains of *M. avium*, *M. intracellulare* and *M. scrofulaceum* and all strains closely related to the above mentioned species and not clearly belonging to another defined *Mycobacterium* species. The latter group of strains are defined in this invention as "MIC strains" (*M. intracellulare* complex).

[0133] Preferentially, at least two, three, four, five, six, seven, eight or more of said probes are used simultaneously.

[0134] In still another specific embodiment, the invention provides for a method as described above, to detect and identify one or more *M. avium* and *M. paratuberculosis* strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

50 MAV-ICG-1 : TCGGTCCGTCCGTGTGGAGTC (SEQ ID NO 10)

MAV-ICG-22 : GTGGCCGGCGTTCATCGAAA (SEQ ID NO 11)

55

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 77 and 78 provided said probe hybridizes specifically to *M. avium* or *M. paratuberculosis*.

[0135] The sequences as represented in SEQ ID NO 77 and 78 are new.

[0136] Preferentially, this embodiment uses both probes in combination.

[0137] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium intracellulare strains and MIC-strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

	MAI-ICG-1 :	CAACAGCAAATGATTGCCAGACACAC	(SEQ ID NO 6)
10	MIL-ICG-11 :	GAGGGGTTCCCGTCTGTAGTG	(SEQ ID NO 7)
	MIL-ICG-22 :	TGAGGGGTTCTCGTCTGTAGTG	(SEQ ID NO 8)
	MAC-ICG-1 :	CACTCGGTCGATCCGTGTGGA	(SEQ ID NO 9)
15	MIN-ICG-1 :	GCATAGTCCTTAGGGCTGATGCGTT	(SEQ ID NO 12)
	MIN-ICG-2 :	GCTGATGCGTTCGTCGAAATGTGTA	(SEQ ID NO 13)
	MIN-ICG-22 :	CTGATGCGTTCGTCGAAATGTGT	(SEQ ID NO 14)
20	MIN-ICG-222 :	TGATGCGTTCGTCGAAATGTGT	(SEQ ID NO 15)
	MIN-ICG-2222 :	GGCTGATGCGTTCGTCGAAATGTGTAA	(SEQ ID NO 16)
25	MAL-ICG-1 :	ACTAGATGAACGCGTAGTCCTTGT	(SEQ ID NO 17)
	MHEF-ICG-1 :	TGGACGAAAACCGGGTGCACAA	(SEQ ID NO 18)
	MAH-ICG-1 :	GTGTAATTTCTTTTTTAACTCTTGTGTGTAAGTAAGTG	(SEQ ID NO 19)
30	MCO-ICG-11 :	TGGCCGGCGTGTTTCATCGAAA	(SEQ ID NO 20)
	MTH-ICG-11 :	GCACTTCAATTGGTGAAGTGCGAGCC	(SEQ ID NO 21)
35	MTH-ICG-2 :	GCGTGGTCTTCATGGCCGG	(SEQ ID NO 22)
	MEF-ICG-11 :	ACGCGTGGTCCTTCGTGG	(SEQ ID NO 23)

or to equivalents of said probes,

40 and/or to any probe derived from SEQ ID NO 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99 provided said probe hybridizes specifically to M. intracellulare strains and MIC-strains.

[0138] The sequences as represented in SEQ ID NO 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99 are new.

[0139] Preferentially, at least two, three, four, five, six, seven, eight or more of said probes are used simultaneously.

45 [0140] In still another specific embodiment, the invention provides for a method as described above, to detect and identify one or more Mycobacterium intracellulare strains in a sample, wherein step (iii) comprises hybridizing to at least the following probes :

50	MIN-ICG-1 :	GCATAGTCCTTAGGGCTGATGCGTT	(SEQ ID NO 12)
----	-------------	---------------------------	----------------

or to equivalents of said probe,

and/or to any probe derived from SEQ ID NO 89 provided said probe hybridizes specifically to M. intracellulare strains.

55 [0141] In still another specific embodiment, the invention provides for a method as described above, to detect and identify one or more Mycobacterium scrofulaceum strains in a sample, wherein step (iii) comprises hybridizing to the following probe:



MSC-ICG-1 : TCGGCTCGTTCTGAGTGGTGTC

(SEQ ID NO 24)

or to equivalents of said probes,

5 and/or to any probe derived from SEQ ID NO 100 provided said probe hybridizes specifically to M. scrofulaceum.

[0142] The sequence as represented in SEQ ID NO 100 is new.

[0143] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium kansasii strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

10

MKA-ICG-1 : GATGCGTTTGCTACGGGTAGCGT (SEQ ID NO 25)

MKA-ICG-2 : GATGCGTTGCCTACGGGTAGCGT (SEQ ID NO 26)

15 MKA-ICG-3 : ATGCGTTGCCCTACGGGTAGCGT (SEQ ID NO 27)

MKA-ICG-4 : CGGGCTCTGTTCGAGAGTTGTC (SEQ ID NO 28)

MKA-ICG-5 : CCCTCAGGGATTTTCTGGGTGTTG (SEQ ID NO 182)

20 MKA-ICG-6 : GGACTCGTCCAAGAGTGTTGTCC (SEQ ID NO 183)

MKA-ICG-7 : TCGGGCTTGGCCAGAGCTGTT (SEQ ID NO 184)

25 MKA-ICG-8 : GGGTGCGCAACAGCAAGCGA (SEQ ID NO 185)

MKA-ICG-9 : GATGCGTTGCCCCTACGGG (SEQ ID NO 186)

MKA-ICG-10 : CCCTACGGGTAGCGTGTTCTTTTG (SEQ ID NO 187)

30 and more preferably to :

MKA-ICG-3 : ATGCGTTGCCCTACGGGTAGCGT (SEQ ID NO 27)

35 MKA-ICG-4 : CGGGCTCTGTTCGAGAGTTGTC (SEQ ID NO 28)

MKA-ICG-5 : CCCTCAGGGATTTTCTGGGTGTTG (SEQ ID NO 182)

40 MKA-ICG-6 : GGACTCGTCCAAGAGTGTTGTCC (SEQ ID NO 183)

MKA-ICG-7 : TCGGGCTTGGCCAGAGCTGTT (SEQ ID NO 184)

MKA-ICG-8 : GGGTGCGCAACAGCAAGCGA (SEQ ID NO 185)

45 MKA-ICG-9 : GATGCGTTGCCCCTACGGG (SEQ ID NO 186)

MKA-ICG-10 : CCCTACGGGTAGCGTGTTCTTTTG (SEQ ID NO 187)

50 or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 101, 167, 168 or 169 provided said probe hybridizes specifically to M. kansasii.

[0144] The sequences as represented in SEQ ID NO 101, 167, 168 and 169 are new.

[0145] Preferentially, at least two, three or four of said probes are used simultaneously.

55 [0146] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium chelonae strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

MCH-ICG-1 : GGTGTGGACTTTGACTTCTGAATAG (SEQ ID NO 29)  
 MCH-ICG-2 : CGGCAAAACGTCGGACTGTCA (SEQ ID NO 30)  
 5 MCH-ICG-3 : GGTGTGGTCCTTGACTTATGGATAG (SEQ ID NO 210)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 102, 103 or 174 provided said probe hybridizes specifically to M. chelonae.  
 10 According to another preferential embodiment, these three probes are used in combination.

[0147] The sequences as represented in SEQ ID NO 102, 103 and 174 are new.

[0148] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium gordonae strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

15 MGO-ICG-1 : AACACCCTCGGGTGCTGTCC (SEQ ID NO 31)  
 MGO-ICG-2 : GTATGCGTTGTCGTTGCGGGC (SEQ ID NO 32)  
 20 MGO-ICG-5 : CGTGAGGGGTCATCGTCTGTAG (SEQ ID NO 33)

and more preferably to:

25 MGO-ICG-5 : CGTGAGGGGTCATCGTCTGTAG (SEQ ID NO 33)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 104, 105 or 106 provided said probe hybridizes specifically to M. gordonae.

[0149] The sequences as represented in SEQ ID NO 104 to 106 are new.

30 [0150] Preferentially, at least two or three of said probes are used simultaneously.

[0151] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium ulcerans strains or Mycobacterium marinum strains in a sample, wherein step (iii) comprises hybridizing to the following probe:

35 MUL-ICG-1 : GGTTTCGGGATGTTGTCCCACC (SEQ ID NO 175)

or to equivalents of said probe,

and/or to any probe derived from SEQ ID NO 157 provided said probe hybridizes specifically to M. ulcerans and M. marinum.

40 [0152] The sequence as represented in SEQ ID NO 157 is new.

[0153] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium genavense strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

45 MGV-ICG-1 : CGACTGAGGTCGACGTGGTGT (SEQ ID NO 176)  
 MGV-ICG-2 : GGTGTTTGAGCATTGAATAGTGGTTGC (SEQ ID NO 177)  
 50 MGV-ICG-3 : TCGGGCCGCGTGTTCGTCAA (SEQ ID NO 211)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 158, 159, 160, 161 or 162 provided said probe hybridizes specifically to M. genavense.

55 [0154] The sequences as represented in SEQ ID NO 158 to 162 are new.

[0155] As described in the examples, M. genavense includes M. genavense strains sensu strictu and a group of closely related strains called M. simiae-like. The former group of strains can be detected specifically with probe MGV-

ICG-1 while the latter group hybridizes specifically with probe MGV-ICG-3. Probe MGV-ICG-2 detects both groups.

[0156] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium xenopi strains in a sample, wherein step (iii) comprises hybridizing to the following probe:

5 MXE-ICG-1 : GTTGGGCAGCAGGCAGTAACC (SEQ ID NO 178)

10 or to equivalents of said probe,

and/or to any probe derived from SEQ ID NO 163 provided said probe hybridizes specifically to M. xenopi.

[0157] The sequence as represented in SEQ ID NO 163 is new.

[0158] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium simiae strains in a sample, wherein step (iii) comprises hybridizing to the following probe:

15 MSI-ICG-1 : CCGGCAACGGTTACGTGTTC (SEQ ID NO 179)

20 or to equivalents of said probe,

and/or to any probe derived from SEQ ID NO 164 or 165 provided said probe hybridizes specifically to M. simiae.

[0159] The sequence as represented in SEQ ID NO 164 or 165 is new.

[0160] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium fortuitum strains in a sample, wherein step (iii) comprises hybridizing to at least one of the the following probes:

25 MFO-ICG-1 : TCGTTGGATGGCCTCGCACCT (SEQ ID NO 180)

30 MFO-ICG-2 : ACTTGGCGTGGGATGCGGGAA (SEQ ID NO 181)

or to equivalents of said probes or to any probe derived from SEQ ID NO 166 provided said probe hybridizes specifically to M. fortuitum.

[0161] The sequence as represented in SEQ ID NO 166 is new.

35 [0162] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium celatum strains in a sample, wherein step (iii) comprises hybridizing to the following probe:

40 MCE-ICG-1 : TGAGGGAGCCCGTGCCTGTA (SEQ ID NO 190)

or to equivalents of said probe,

and/or to any probe derived from SEQ ID NO 170 provided said probe hybridizes specifically to M. celatum.

[0163] The sequence as represented in SEQ ID NO 170 is new.

45 [0164] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium haemophilum strains in a sample, wherein step (iii) comprises hybridizing to the following probe:

50 MHP-ICG-1 : CATGTTGGGCTTGATCGGGTGC (SEQ ID NO 191)

or to equivalents of said probe,

and/or to any probe derived from SEQ ID NO 171, 172 or 173 provided said probe hybridizes specifically to M. haemophilum.

55 [0165] The sequences as represented in SEQ ID NO 171 to 173 are new.

[0166] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium malmoense strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

MML-ICG-1 : CGGATCGATTGAGTGCTTGTCCC (SEQ ID NO 188)

MML-ICG-2 : TCTAAATGAACGCACTGCCGATGG (SEQ ID NO 189)

5

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 107 provided said probe hybridizes specifically to M. malmoeense.

[0167] The sequence as represented in SEQ ID NO 107 is new.

10

[0168] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

15

MYC-ICG-1 : ACTGGATAGTGGTTGCGAGCATCTA (SEQ ID NO 1)

MYC-ICG-22 : CTTCTGAATAGTGGTTGCGAGCATCT (SEQ ID NO 2)

or to equivalents of said probes.

20

[0169] According to a preferred embodiment, both probes are used in combination.

[0170] The invention also provides for a method as described above to detect and identify one or more Mycoplasma strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

25

MPN-ICG 1 : ATCGGTGGTAAATTAAACCCAAATCCCTGT (SEQ ID NO 49)

MPN-ICG 2 : CAGTTCTGAAAGAACATTTCCGCTTCTTTC (SEQ ID NO 50)

MGE-ICG 1 : CACCCATTAATTTTTTCGGTGTTAAAACCC (SEQ ID NO 51)

30

Mycoplasma-ICG : CAAAACTGAAAACGACAATCTTTCTAGTTCC (SEQ ID NO 52)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 124 or 125 provided said probe hybridizes specifically with Mycoplasma species.

35

[0171] Preferentially, at least two, three or four of said probes are used simultaneously.

[0172] More particularly, the invention provides for a method as described above to detect and identify one or more Mycoplasma pneumoniae strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

40

MPN-ICG 1 : ATCGGTGGTAAATTAAACCCAAATCCCTGT (SEQ ID NO 49)

MPN-ICG 2 : CAGTTCTGAAAGAACATTTCCGCTTCTTTC (SEQ ID NO 50)

45

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 125 provided said probe hybridizes specifically to Mycoplasma pneumoniae. According to a preferred embodiment, both these probes are used in combination.

[0173] The sequence as represented in SEQ ID NO 125 is new.

50

[0174] In another particular embodiment, the invention provides for a method as described above to detect and identify one or more Mycoplasma genitalium strains in a sample, wherein step (iii) comprises hybridizing to the following probe:

55

MGE-ICG 1 : CACCCATTAATTTTTTCGGTGTTAAAACCC (SEQ ID NO 51)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 124 provided said probe hybridizes specifically to Mycoplasma genitalium.

[0175] The sequence as represented in SEQ ID NO 124 is new.

[0176] The invention also provides for a method as described above to detect and identify one or more Pseudomonas strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

- 5 PA-ICG 1 : TGGTGTGCTGCGTGATCCGAT (SEQ ID NO 34)  
 PA-ICG 2 : TGAATGTTCGTGGATGAACATTGATT (SEQ ID NO 35)  
 PA-ICG 3 : CACTGGTGATCATTCAAGTCAAG (SEQ ID NO 36)  
 10 PA-ICG 4 : TGAATGTTCGT(G/A)(G/A)ATGAACATTGATTTCTGGTC  
 (SEQ ID NO 37)  
 PA-ICG 5 : CTCTTTCACTGGTGATCATTCAAGTCAAG (SEQ ID NO 38)

15 or to equivalents of said probes,  
 and/or to any probe derived from SEQ ID NO 111, 112, 113, 114 or 115 provided said probe hybridizes specifically to Pseudomonas strains.

[0177] The sequences as represented in SEQ ID NO 111 to 115 are new.

20 [0178] Preferentially, at least two, three or four of said probes are used simultaneously.

[0179] More particularly, the invention provides for a method as described above to detect and identify one or more Pseudomonas aeruginosa strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

- 25 PA-ICG 1 : TGGTGTGCTGCGTGATCCGAT (SEQ ID NO 34)  
 PA-ICG 2 : TGAATGTTCGTGGATGAACATTGATT (SEQ ID NO 35)  
 PA-ICG 3 : CACTGGTGATCATTCAAGTCAAG (SEQ ID NO 36)  
 30 PA-ICG 4 : TGAATGTTCGT(G/A)(G/A)ATGAACATTGATTTCTGGTC  
 (SEQ ID NO 37)  
 PA-ICG 5 : CTCTTTCACTGGTGATCATTCAAGTCAAG (SEQ ID NO 38)

35 and most preferably to at least one of the following probes:

- 40 PA-ICG 1 : TGGTGTGCTGCGTGATCCGAT (SEQ ID NO 34)  
 PA-ICG 4 : TGAATGTTCGT(G/A)(G/A)ATGAACATTGATTTCTGGTC  
 (SEQ ID NO 37)  
 PA-ICG 5 : CTCTTTCACTGGTGATCATTCAAGTCAAG (SEQ ID NO 38)

45 or to equivalents of said probes,  
 and/or to any probe derived from SEQ ID NO 111 provided said probe hybridizes specifically to Pseudomonas aeruginosa.

[0180] The sequence as represented in SEQ ID NO 111 is new.

50 [0181] Preferentially, at least two, three, four or five of said probes are used simultaneously.

[0182] The invention also provides for a method as described above to detect and identify one or more Staphylococcus species in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

55

STAU-ICG 1 : TACCAAGCAAAACCGAGTGAATAAAGAGTT (SEQ ID NO 53)

STAU-ICG 2 : CAGAAGATGCGGAATAACGTGAC (SEQ ID NO 54)

5 STAU-ICG 3 : AACGAAGCCGTATGTGAGCATTTGAC (SEQ ID NO 55)

STAU-ICG 4 : GAACGTAACCTTCATGTTAACGTTTGACTTAT (SEQ ID NO 56)

or to equivalents of said probes,

10 and/or to any probe derived from SEQ ID NO 139, 140, 141, 142, 143 or 144 provided said probe hybridizes specifically to Staphylococcus species.

[0183] The sequences as represented in SEQ ID NO 139 to 144 are new.

[0184] Preferentially, at least two, three or four of said probes are used simultaneously.

15 [0185] More particularly, the invention provides for a method as described above to detect and identify one or more Staphylococcus aureus strains in a sample, wherein step (iii) comprises hybridizing to at least one, and preferably both of the following probes:

20 STAU-ICG 3 : AACGAAGCCGTATGTGAGCATTTGAC (SEQ ID NO 55)

STAU-ICG 4 : GAACGTAACCTTCATGTTAACGTTTGACTTAT (SEQ ID NO 56)

or to equivalent of said probes,

25 and/or to any probe derived from SEQ ID NO 139, 140, 141, 142, or 143 provided said probe hybridizes specifically to Staphylococcus aureus. According to a preferred embodiment, both these probes are used in combination.

[0186] In another specific embodiment the invention provides for a method as described above to detect and identify one or more Staphylococcus epidermidis strains in a sample, wherein step (iii) comprises hybridizing to any probe derived from SEQ ID NO 144 as long as this probe can be caused to hybridize specifically to Staphylococcus epidermidis.

30 [0187] The invention also provides for a method as described above to detect and identify one or more Acinetobacter strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

35 ACI-ICG 1 : GCTTAAGTGCACAGTGCTCTAAACTGA (SEQ ID NO 57)

ACI-ICG 2 : CACGGTAATTAGTGTGATCTGACGAAG (SEQ ID NO 58)

or to equivalents of said probes,

40 and/or to any probe derived from SEQ ID NO 126, 127, 128, 129 or 130 provided said probe hybridizes specifically to Acinetobacter sp.. According to a preferred embodiment, both these probes are used in combination.

[0188] The sequences as represented in SEQ ID NO 126 to 130 are new.

45 [0189] More particularly, the invention provides for a method as described above to detect and identify one or more Acinetobacter baumannii strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

50 ACI-ICG 1 : GCTTAAGTGCACAGTGCTCTAAACTGA (SEQ ID NO 57)

ACI-ICG 2 : CACGGTAATTAGTGTGATCTGACGAAG (SEQ ID NO 58)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 126 provided said probe hybridizes specifically to Acinetobacter baumannii. According to a preferred embodiment, both these probes are used in combination.

55 [0190] The invention also provides for a method as described above, to detect and identify one or more Listeria strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

LIS-ICG 1 : CAAGTAACCGAGAATCATCTGAAAGTGAATC (SEQ ID NO 39)

LMO-ICG 1 : AAACAACCTTTACTTCGTAGAAGTAAATTGGTTAAG

5 (SEQ ID NO 40)

LMO-ICG 2 : TGAGAGGTTAGTACTTCTCAGTATGTTTGTTT (SEQ ID NO 41)

LMO-ICG 3 : AGGCACTATGCTTGAAGCATCGC (SEQ ID NO 42)

10 LIV-ICG 1 : GTTAGCATAAATAGGTAAGTATTTATGACACAAGTAAC  
(SEQ ID NO 43)

LSE-ICG 1 : AGTTAGCATAAGTAGTGTAAGTATTTATGACACAAG

15 LISP-ICG 1 : CGTTTTTCATAAGCGATCGCACGTT (SEQ ID NO 212)

and most preferably to at least one of the following probes:

20 LIS-ICG 1 : CAAGTAACCGAGAATCATCTGAAAGTGAATC (SEQ ID NO 39)

LMO-ICG 3 : AGGCACTATGCTTGAAGCATCGC (SEQ ID NO 42)

25 LISP-ICG 1 : CGTTTTTCATAAGCGATCGCACGTT (SEQ ID NO 212)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 116, 118, 119, 120, 121, 213, 214 or 215 provided said probe hybridizes specifically to *Listeria* species.

30 [0191] As described in the examples section, *Listeria* species encompass *Listeria* species sensu strictu, and a group of closely related organisms referred to as "Listeria-like organisms". The latter group can be specifically recognized by probe LISP-ICG 1.

[0192] The sequences as represented in SEQ ID NO 116, 118 to 121 and 213 to 215 are new.

[0193] Preferentially, at least two, three, four, five or six of said probes are used simultaneously.

35 [0194] More particularly, the invention provides for a method as described above, to detect and identify one or more *Listeria monocytogenes* strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

40 LMO-ICG 1 : AAACAACCTTTACTTCGTAGAAGTAAATTGGTTAAG (SEQ ID NO 40)

LMO-ICG 2 : TGAGAGGTTAGTACTTCTCAGTATGTTTGTTT (SEQ ID NO 41)

LMO-ICG 3 : AGGCACTATGCTTGAAGCATCGC (SEQ ID NO 42)

45 and most preferably to the following probe:

LMO-ICG 3 : AGGCACTATGCTTGAAGCATCGC (SEQ ID NO 42)

50

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 120 provided said probe hybridizes specifically to *Listeria monocytogenes*.

[0195] Preferentially, at least two, or three of said probes are used simultaneously.

55 [0196] The invention also provides for a method as described above to detect and identify one or more *Brucella* strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

BRU-ICG 1 : CGTGCCGCCTTCGTTTCTCTTT (SEQ ID NO 59)  
 BRU-ICG 2 : TTCGCTTCGGGGTGGATCTGTG (SEQ ID NO 60)  
 5 BRU-ICG 3 : GCGTAGTAGCGTTTGCGTCGG (SEQ ID NO 193)  
 BRU-ICG 4 : CGCAAGAAGCTTGCTCAAGCC (SEQ ID NO 194)

and most preferably to at least one of the following probes:

10 BRU-ICG 2 : TTCGCTTCGGGGTGGATCTGTG (SEQ ID NO 60)  
 15 BRU-ICG 3 : GCGTAGTAGCGTTTGCGTCGG (SEQ ID NO 193)  
 BRU-ICG 4 : CGCAAGAAGCTTGCTCAAGCC (SEQ ID NO 194)

or to equivalents of said probes,

20 and/or to any probe derived from SEQ ID NO 131, 132 or 154 provided said probe hybridizes specifically to Brucella strains.

[0197] The sequences as represented in SEQ ID NO 131, 132 and 154 are new.

[0198] The invention also provides for a method as described above to detect and identify one or more Salmonella strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

25 SALM-ICG 1 : CAAAACTGACTTACGAGTCACGTTTGAG (SEQ ID NO 61)  
 SALM-ICG 2 : GATGTATGCTTCGTTATTCCACGCC (SEQ ID NO 62)  
 30 STY-ICG 1 : GGTCAAACCTCCAGGGACGCC (SEQ ID NO 63)  
 SED-ICG 1 : GCGGTAATGTGTGAAAGCGTTGCC (SEQ ID NO 64)

and most preferably to the following probe:

35 SALM-ICG 1 : CAAAACTGACTTACGAGTCACGTTTGAG (SEQ ID NO 61)

or to equivalents of said probes,

40 and/or to any probe derived from SEQ ID NO 133, 134, 135, 136, 137 or 138 provided said probe hybridizes specifically to Salmonella strains.

[0199] The sequences as represented in SEQ ID NO 133 to 138 are new.

[0200] Preferentially, at least two, three, or four of said probes are used simultaneously.

45 [0201] The invention also relates to a method as described above to detect and identify one or more Chlamydia strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

CHTR-ICG 1 : GGAAGAAGCCTGAGAAGGTTTCTGAC (SEQ ID NO 45)  
 50 CHTR-ICG 2 : GCATTTATATGTAAGAGCAAGCATTCTATTCA (SEQ ID NO 46)  
 CHTR-ICG 3 : GAGTAGCGTGGTGAGGACGAGA (SEQ ID NO 47)  
 CHTR-ICG 4 : GAGTAGCGCGGTGAGGACGAGA (SEQ ID NO 201)  
 55 CHPS-ICG 1 : GGATAACTGTCTTAGGACGGTTTGAC (SEQ ID NO 48)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 122, 123 or 197 provided that said probe hybridizes specifically to Chlamy-



dia strains.

[0202] Preferentially, at least two, three, four or five of said probes are used simultaneously.

[0203] More particularly, the invention relates to a method as described above to detect and identify one or more Chlamydia trachomatis strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

CHTR-ICG 1 : GGAAGAAGCCTGAGAAGGTTTCTGAC (SEQ ID NO 45)

CHTR-ICG 2 : GCATTTATATGTAAGAGCAAGCATTCTATTTC (SEQ ID NO 46)

CHTR-ICG 3 : GAGTAGCGTGGTGAGGACGAGA (SEQ ID NO 47)

CHTR-ICG 4 : GAGTAGCGCGGTGAGGACGAGA (SEQ ID NO 201)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 123 or 197 provided said probe hybridizes specifically to Chlamydia trachomatis.

[0204] The sequences as represented in SEQ ID NO 123 and 197 are new.

[0205] Preferentially, at least two, three or four of said probes are used simultaneously.

[0206] In another particular embodiment, the invention provides for a method as described above to detect and identify one or more Chlamydia psittaci strains in a sample, wherein step (iii) comprises hybridizing to at least the following probe:

CHPS-ICG 1 : GGATAACTGTCTTAGGACGGTTTGAC (SEQ ID NO 48)

or to equivalents of said probe,

and/or to any probe derived from SEQ ID NO 122 provided said probe hybridizes specifically to Chlamydia psittaci.

[0207] The sequence of SEQ ID NO 122 is new.

[0208] The invention also provides for a method as described above, to detect one or more Streptococcus strains in a sample, wherein step (iii) comprises hybridizing to any probe derived from SEQ ID NO 145, 146, 147, 148, 149, 150, 151, 152 or 153 provided said probe hybridizes specifically to Streptococcus strains, or equivalents of these probes.

[0209] The sequences as represented in SEQ ID NO 145, 146, 147, 148, 149, 150, 151, 152 or 153 are new.

[0210] The invention also provides for a method as described above, to detect one or more Yersinia enterocolitica strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes :

YEC-ICG 1 : GGAAAAGGTACTGCACGTGACTG (SEQ ID NO 198)

YEC-ICG 2 : GACAGCTGAACTTATCCCTCCG (SEQ ID NO 199)

YEC-ICG 3 : GCTACCTGTTGATGTAATGAGTCAC (SEQ ID NO 200)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 195 or 196, provided said probe hybridizes specifically to Yersinia enterocolitica.

[0211] The sequences as represented in SEQ ID NO 195 and 196 are new.

[0212] In some cases it may be advantageous to amplify not all organisms present in a sample, but only more specific taxa, which are considered to be relevant. In these cases the invention provides for primers allowing the specific amplification of the spacer region for only those beforehand defined taxa.

[0213] The invention thus provides for a method as described above to detect and identify specifically Chlamydia trachomatis in a sample, wherein step (ii) comprises amplification of the 16S-23S rRNA spacer region or a part of it, using at least one of the following primers:

CHTR-P1 : AAGGTTTCTGACTAGGTTGGGC (SEQ ID NO 69)

CHTR-P2 : GGTGAAGTGCTTGCATGGATCT (SEQ ID NO 70)

5

or equivalents of these primers, said equivalents differing in sequence from the above mentioned primers by changing one or more nucleotides, provided that said equivalents still amplify specifically the spacer region or part of it from *Chlamydia trachomatis*.

[0214] Preferably both primers are used.

10

[0215] The invention also provides for a method as described above to detect and identify specifically *Listeria* species in a sample, wherein step (ii) comprises amplification of the 16S-23S rRNA spacer region or a part of it, using at least one of the following primers:

15

LIS-P1 : ACCTGTGAGTTTTTCGTTCTTCTC (SEQ ID NO 71)

LIS-P2 : CTATTTGTTCAAGTTTTGAGAGGTT (SEQ ID NO 72)

LIS-P3 : ATTTTCCGTATCAGCGATGATAC (SEQ ID NO 73)

20

LIS-P4 : ACGAAGTAAAGGTTGTTTTTCT (SEQ ID NO 74)

LIS-P5 : GAGAGGTTACTCTCTTTTATGTCAG (SEQ ID NO 75)

LIS-P6 : CTTTTATGTCAGATAAAGTATGCAA (SEQ ID NO 202)

25

LIS-P7 : CGTAAAAGGGTATGATTATTTG (SEQ ID NO 203)

or equivalents of these primers, said equivalents differing in sequence from the above mentioned primers by changing one or more nucleotides, provided that said equivalents still amplify specifically the spacer region or part of it from *Listeria* species.

30

[0216] The invention also relates to a method as described above to detect and identify specifically *Mycobacterium* species in a sample, wherein step (ii) comprises amplification of the 16S-23S rRNA spacer region or a part of it, using at least one of the following primers:

35

MYC-P1: TCCCTTGTGGCCTGTGTG (SEQ ID NO 65)

MYC-P2: TCCTTCATCGGCTCTCGA (SEQ ID NO 66)

40

MYC-P3: GATGCCAAGGCATCCACC (SEQ ID NO 67)

MYC-P4: CCTCCCACGTCCTTCATCG (SEQ ID NO 68)

45

MYC-P5: CCTGGGTTTGACATGCACAG (SEQ ID NO 192)

or equivalents of these primers, said equivalents differing in sequence from the above mentioned primers by changing one or more nucleotides, provided that said equivalents still amplify specifically the spacer region or part of it from *Mycobacterium* species.

50

[0217] The invention also provides for a method as described above to detect and identify specifically *Brucella* species in a sample, wherein step (ii) comprises amplification of the 16S-23S rRNA spacer region or part of it, using at least one of the following primers :

55

BRU-P1 : TCGAGAATTGGAAAGAGGTC (SEQ ID NO 204)  
 BRU-P2 : AAGAGGTCGGATTTATCCG (SEQ ID NO 205)  
 5 BRU-P3 : TTCGACTGCAAATGCTCG (SEQ ID NO 206)  
 BRU-P4 : TCTTAAAGCCGCATTATGC (SEQ ID NO 207)

or equivalents of these primers, said equivalents differing in sequence from the above-mentioned primers by changing one or more nucleotides, provided that said equivalents still amplify specifically the spacer region of part of it from *Brucella* species.

[0218] The invention also provides for a method as described above to detect and identify specifically *Yersinia enterocolitica* species in a sample, wherein step (ii) comprises amplification of the 16S-23S rRNA spacer region or part of it, using at least one of the following primers :

YEC-P1 : CCTAATGATATTGATTCGCG (SEQ ID NO 208)  
 YEC-P2 : ATGACAGGTTAATCCTTACCCC (SEQ ID NO 209)

or equivalents of these primers, said equivalents differing in sequence from the above-mentioned primers by changing one or more nucleotides, provided that said equivalents still amplify specifically the spacer region of part of it from *Yersinia enterocolitica* species.

[0219] The invention also provides for a composition comprising at least one of the probes and/or primers as defined above.

[0220] Said composition may comprise any carrier, support, label or diluent known in the art for probes or primers, more particularly any of the labels or supports detailed in the definitions section.

[0221] The invention relates more particularly to isolated probes and primers as defined above, more particularly any of the probes as specified in Table 1a or any of the primers as specified in Table 1b.

[0222] According to another embodiment, the present invention relates also to new spacer region sequences as defined above and as set out in figures 1-103 (SEQ ID NO 76 to 154, SEQ ID NO 157 to 174, SEQ ID NO 195 to 197 and SEQ ID NO 213 to 215).

[0223] In another embodiment the invention provides for a reverse hybridization method comprising any of the probes as defined above, wherein said probes are immobilized on a known location on a solid support, more preferably on a membrane strip.

[0224] In yet another embodiment the invention provides for a kit for the detection and identification of at least one micro-organism, or the simultaneous detection and identification of several micro-organisms in a sample, comprising the following components:

- (i) when appropriate, at least one suitable primer pair to allow amplification of the intercistronic 16S-23S rRNA spacer region, or a part of it;
- (ii) at least one of the probes as defined above;
- (iii) a buffer, or components necessary to produce the buffer, enabling a hybridization reaction between said probes and the polynucleic acids present in the sample, or the amplified products thereof;
- (iv) a solution, or components necessary to produce the solution, enabling washing of the hybrids formed under the appropriate wash conditions;
- (v) when appropriate, a means for detecting the hybrids resulting from the preceding hybridization.

#### FIGURE LEGENDS

[0225]

Fig 1 : represents the DNA sequence of the 16S-23S rRNA spacer region from *Mycobacterium tuberculosis* strain H37RV ATCC 27294 (SEQ ID NO 76)

Fig 2: represents the DNA sequence of the 16S-23S rRNA spacer region from *Mycobacterium avium* ATCC 151.769 (ITG 4991) (SEQ ID NO 77)

- Fig 3: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium paratuberculosis strains 316F and 2E (SEQ ID NO 78)
- 5 Fig 4: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 5513 (SEQ ID NO 79)
- Fig 5: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 8695 (SEQ ID NO 80)
- 10 Fig 6: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 8708 (SEQ ID NO 81).
- Fig 7: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 8715 (SEQ ID NO 82).
- 15 Fig 8: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 8054 (SEQ ID NO 83)
- Fig 9: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 8737 (SEQ ID NO 84)
- 20 Fig 10: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 8743 (SEQ ID NO 85)
- Fig 11: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 8745 (SEQ ID NO 86)
- 25 Fig 12: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 8748 (SEQ ID NO 87)
- 30 Fig 13: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 8752 (SEQ ID NO 88)
- Fig 14: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium intracellulare serovar 12 ITG 5915 (SEQ ID NO 89)
- 35 Fig 15: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium lufu ITG 4755 (SEQ ID NO 90)
- Fig 16: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 5922 (SEQ ID NO 91)
- 40 Fig 17: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 1329 (SEQ ID NO 92)
- 45 Fig 18: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 1812 (SEQ ID NO 93)
- Fig 19: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 5280 (SEQ ID NO 94)
- 50 Fig 20: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 5620 (SEQ ID NO 95)
- Fig 21: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 5765 (SEQ ID NO 96)
- 55 Fig 22: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium ITG 7395 (SEQ

ID NO 97)

- Fig 23 represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium ITG 8738 (SEQ ID NO 98)
- 5 Fig 24 : represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium ITG 926 (SEQ ID NO 99)
- 10 Fig 25: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium scrofulaceum ITG 4988 (SEQ ID NO 100)
- Fig 26: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium kansasii ATCC 22478 (=ITG 4987) (SEQ ID NO 101)
- 15 Fig 27 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium chelonae abscessus ITG 4975 (SEQ ID NO 102)
- Fig 28 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium chelonae chelonae ITG 9855 (SEQ ID NO 103)
- 20 Fig 29 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium gordonae ITG 7703 (SEQ ID NO 104)
- Fig 30 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium gordonae ITG 7836 (SEQ ID NO 105)
- 25 Fig 31 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium gordonae ITG 8059 (SEQ ID NO 106)
- 30 Fig 32 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium malmoeense ITG 4842 and ITG 4832 (SEQ ID NO 107)
- Fig 33: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium strain 8757 (SEQ ID NO 108)
- 35 Fig 34 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium ITG 8723 (SEQ ID NO 109)
- Fig 35 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium ITG 8724 (SEQ ID NO 110)
- 40 Fig 36 : represents the DNA sequence of the 16S-23S spacer region from Pseudomonas aeruginosa UZG 5669 (SEQ ID NO 111)
- 45 Fig 37 : represents the DNA sequence of the 16S-23S spacer region from Pseudomonas pseudoalcaligenes LMG 1225 (SEQ ID NO 112)
- Fig 38 : represents the DNA sequence of the 16S-23S spacer region from Pseudomonas stutzeri LMG 2333 (SEQ ID NO 113)
- 50 Fig 39: represents the DNA sequence of the 16S-23S spacer region from Pseudomonas alcaligenes LMG 1224 (SEQ ID NO 114)
- Fig 40 : represents the DNA sequence of the 16S-23S spacer region from Pseudomonas putida LMG 2232 (SEQ ID NO 115)
- 55 Fig 41: represents the DNA sequence of the small 16S-23S spacer region from Listeria ivanovii CIP 7842 (SEQ ID NO 116)

- Fig 42 : represents the DNA sequence of the small 16S-23S spacer region from Listeria monocytogenes (SEQ ID NO 117)
- 5 Fig 43 : represents the DNA sequence of the small 16S-23S spacer region from Listeria seeligeri serovar 4A nr. 4268 (SEQ ID NO 118)
- Fig 44 : represents the partial DNA sequence of the large 16S-23S spacer region from partial sequence of the long spacer region of Listeria ivanovii CIP 7842 (SEQ ID NO 119)
- 10 Fig 45: represents the DNA sequence of the large 16S-23S spacer region from Listeria monocytogenes IHE serovar 4B (SEQ ID NO 120)
- Fig 46 : represents the DNA sequence of the large 16S-23S spacer region from Listeria seeligeri serovar 4A nr. 4268 (SEQ ID NO 121)
- 15 Fig 47 : represents the DNA sequence of the 16S-23S spacer region from Chlamydia psittaci 6BC (SEQ ID NO 122)
- Fig 48 : represents the DNA sequence of the 16S-23S spacer region from Chlamydia trachomatis (SEQ ID NO 123)
- 20 Fig 49 : represents the DNA sequence of the 16S-23S spacer region from Mycoplasma genitalium (U. Gobel) (SEQ ID NO 124)
- Fig 50 : represents the DNA sequence of the 16S-23S spacer region from Mycoplasma pneumoniae ATCC 29432 (SEQ ID NO 125)
- 25 Fig 51 : represents the DNA sequence of the 16S-23S spacer region from Acinetobacter baumanii LMG 1041 (SEQ ID NO 126)
- 30 Fig 52 : represents the DNA sequence of the 16S-23S spacer region from Acinetobacter calcoaceticus LMG 1046 (SEQ ID NO 127)
- Fig 53: represents the DNA sequence of the 16S-23S spacer region from Acinetobacter haemolyticus LMG 996 (SEQ ID NO 128)
- 35 Fig 54 : represents the DNA sequence of the 16S-23S spacer region from Acinetobacter johnsonii LMG 999 (SEQ ID NO 129)
- 40 Fig 55: represents the DNA sequence of the 16S-23S spacer region from Acinetobacter junii LMG 998 (SEQ ID NO 130)
- Fig 56 : represents the DNA sequence of the 16S-23S spacer region from Brucella melitensis NIDO Biovar 1 (SEQ ID NO 131)
- 45 Fig 57 : represents the DNA sequence of the 16S-23S spacer region from Brucella suis NIDO Biovar 1 (SEQ ID NO 132)
- Fig 58 : represents the DNA sequence of one of the 16S-23S spacer region from Salmonella dublin (SEQ ID NO 133)
- 50 Fig 59 : represents the DNA sequence of one of the 16S-23S spacer region from Salmonella dublin (SEQ ID NO 134)
- Fig 60 : represents the DNA sequence of one of the 16S-23S spacer region from Salmonella enteritidis (SEQ ID NO 135)
- 55 Fig 61 : represents the DNA sequence of one of the 16S-23S spacer region from Salmonella enteritidis (SEQ ID

NO 136)

- Fig 62 : represents the DNA sequence of one of the 16S-23S spacer region from Salmonella typhimurium (SEQ ID NO 137)
- 5 Fig 63 : represents the DNA sequence of one of the 16S-23S spacer region from Salmonella typhimurium (SEQ ID NO 138)
- 10 Fig 64 : represents the DNA sequence of one of the 16S-23S spacer region from Staphylococcus aureus strain UZG 5728 (SEQ ID NO 139)
- Fig 65 : represents the DNA sequence of one of the 16S-23S spacer region from Staphylococcus aureus strain UZG 6289 (SEQ ID NO 140)
- 15 Fig 66 : represents the DNA sequence of one of the 16S-23S spacer region from Staphylococcus aureus strain UZG 6289 (SEQ ID NO 141)
- Fig 67 : represents the DNA sequence of one of the 16S-23S spacer region from Staphylococcus aureus strain UZG 6289 (SEQ ID NO 142)
- 20 Fig 68 : represents the DNA sequence of one of the 16S-23S spacer region from Staphylococcus aureus strain UZG 6289 (SEQ ID NO 143)
- 25 Fig 69 : represents the DNA sequence of one of the 16S-23S spacer region from Staphylococcus epidermidis strain UZG CNS41 (SEQ ID NO 144)
- Fig 70 : represents the DNA sequence of the 16S-23S spacer region from Streptococcus mitis UZG 2465 (SEQ ID NO 145)
- 30 Fig 71 : represents the DNA sequence of the 16S-23S spacer region from Streptococcus pyogenes UZG 3671 (SEQ ID NO 146)
- Fig 72 : represents the DNA sequence of the 16S-23S spacer region from Streptococcus sanguis UZG 1042 (SEQ ID NO 147)
- 35 Fig 73 : represents the DNA sequence of the 16S-23S spacer region from Streptococcus saprophyticus UZG CNS46 (SEQ ID NO 148)
- 40 Fig 74 : represents the DNA sequence of the 16S-23S spacer region from Streptococcus species UZG 536 (84) (SEQ ID NO 149)
- Fig 75 : represents the DNA sequence of the 16S-23S spacer region from Streptococcus species UZG 4341 (SEQ ID NO 150)
- 45 Fig 76 : represents the DNA sequence of the 16S-23S spacer region from Streptococcus species UZG 457 (44B) (SEQ ID NO 151)
- Fig 77 : represents the DNA sequence of the 16S-23S spacer region from Streptococcus species UZG 97A (SEQ ID NO 152)
- 50 Fig 78 : represents the DNA sequence of the 16S-23S spacer region from Streptococcus species UZG 483 (76) (SEQ ID NO 153)
- 55 Fig 79 : represents the DNA sequence of the 16S-23S spacer region from Brucella abortus NIDO Tulya biovar 3 (SEQ ID NO 154)
- Fig 80 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium ulcerans ITG 1837 and Mycobacterium marinum ITG 7732 (SEQ ID NO 157)

- Fig 81 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium genavense ITG 8777 (SEQ ID NO 158)
- 5 Fig 82: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium genavense ITG 92-742 (SEQ ID NO 159)
- Fig 83 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium genavense ITG 9500 (SEQ ID NO 160)
- 10 Fig 84 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium simiae-like ITG 7379 (SEQ ID NO 161)
- Fig 85 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium simiae-like ITG 9745 (SEQ ID NO 162)
- 15 Fig 86 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium xenopi ITG 4986 (SEQ ID NO 163)
- Fig 87 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium simiae A ITG 4485 (SEQ ID NO 164)
- 20 Fig 88 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium simiae B ITG 4484 (SEQ ID NO 165)
- Fig 89 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium fortuitum 1 ITG 4304 (SEQ ID NO 166)
- 25 Fig 90 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium kansasii ITG 6328 (SEQ ID NO 167)
- 30 Fig 91 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium kansasii ITG 8698 (SEQ ID NO 168)
- Fig 92 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium kansasii ITG 8973 (SEQ ID NO 169)
- 35 Fig 93 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium celatum ITG 94-123 (SEQ ID NO 170)
- Fig 94: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium haemophilum ITG 776 (SEQ ID NO 171)
- 40 Fig 95 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium haemophilum ITG 778 (SEQ ID NO 172)
- 45 Fig 96 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium haemophilum ITG 3071 (SEQ ID NO 173)
- Fig 97 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium chelonae ITG 94-330 and ITG 94-379 (SEQ ID NO 174)
- 50 Fig 98 : represents the DNA sequence of a 16S-23S spacer region from Yersinia enterocolitica strain P95 (SEQ ID NO 195)
- Fig 99 : represents the DNA sequence of a 16S-23S spacer region from Yersinia enterocolitica strain P95 (SEQ ID NO 196)
- 55 Fig 100: represents the DNA sequence of the 16S-23S spacer region from Chlamydia trachomatis strain SSDZ



94 M 1961 (SEQ ID NO 197)

Fig 101 : represents the DNA sequence of a 16S-23S spacer region from Listeria -like isolate MB 405 (SEQ ID NO 213)

Fig 102 : represents the DNA sequence of a 16S-23S spacer region from Listeria -like isolate MB 405 (SEQ ID NO 214)

Fig 103 : represents the DNA sequence of a 16S-23S spacer region from Listeria -like isolate MB 405 (SEQ ID NO 215)

## TABLE LEGENDS

Table 1a:	List of all new probes originating from the 16S-23S rRNA spacer region
Table 1b:	List of possible primers to be used for taxon-specific amplification of the spacer region or part of it.
Table 2:	Hybridization results for <u>Pseudomonas</u>
Table 3:	Different probe patterns obtained for mycobacterial strain-types
Table 4:	Mycobacteria strains tested in LiPA
Table 5:	Hybridization results for <u>Listeria</u> (Probes LMO1, 2, LSE1, LIV1, LIS1 )
Table 6:	Hybridization results for <u>Listeria</u> (Probes LMO3, LIS1)
Table 7:	Hybridization results for <u>Chlamydia</u>
Table 8:	New mycobacterial probes and hybridization results
Table 9:	Hybridization results for <u>Brucella</u>
Table 10:	Hybridization results for <u>Staphylococcus</u>

**Table 1a**

	<u>PROBE</u>	<u>SEQUENCE</u>	<u>SEQ ID NO</u>
5	MYC-ICG-1	: ACTGGATAGTGGTTGCGAGCATCTA	1
	MYC-ICG-22	: CTTCTGAATAGTGGTTGCGAGCATCT	2
	MTB-ICG-1	: GGGTGCATGACAACAAAGTTGGCCA	3
10	MTB-ICG-2	: GACTTGTTCCAGGTGTTGTCCAC	4
	MTB-ICG-3	: CGGCTAGCGGTGGCGTGTCT	5
	MAI-ICG-1	: CAACAGCAAATGATTGCCAGACACAC	6
15	MIL-ICG-11	: GAGGGGTTCCCGTCTGTAGTG	7
	MIL-ICG-22	: TGAGGGGTTCTCGTCTGTAGTG	8
	MAC-ICG-1	: CACTCGGTCGATCCGTGTGGA	9
20	MAV-ICG-1	: TCGGTCCGTCCGTGTGGAGTC	10
	MAV-ICG-22	: GTGGCCGGCGTTCATCGAAA	11
	MIN-ICG-1	: GCATAGTCCTTAGGGCTGATGCGTT	12
25	MIN-ICG-2	: GCTGATGCGTTCGTCGAAATGTGTA	13
	MIN-ICG-22	: CTGATGCGTTCGTCGAAATGTGT	14
	MIN-ICG-222	: TGATGCGTTCGTCGAAATGTGT	15
30	MIN-ICG-2222	: GGCTGATGCGTTCGTCGAAATGTGTAA	16
	MAL-ICG-1	: ACTAGATGAACGCGTAGTCCTTGT	17
	MHEF-ICG-1	: TGGACGAAAACCGGTGCACAA	18
35	MAH-ICG-1	: GTGTAATTTCTTTTTTA ACTCTTGTGTGTAAGTAAGTG	19
	MCO-ICG-11	: TGGCCGGCGTGTTCATCGAAA	20
	MTH-ICG-11	: GCACTTCAATTGGTGAAGTGCGAGCC	21
40	MTH-ICG-2	: GCGTGGTCTTCATGGCCGG	22
	MEF-ICG-11	: ACGCGTGGTCCTTCGTGG	23
	MSC-ICG-1	: TCGGCTCGTTCGTAGTGGTGTC	24
45	MKA-ICG-1	: GATGCGTTTGCTACGGGTAGCGT	25
	MKA-ICG-2	: GATGCGTTGCCCTACGGGTAGCGT	26
	MKA-ICG-3	: ATGCGTTGCCCTACGGGTAGCGT	27
50	MKA-ICG-4	: CGGGCTCTGTTGAGAGTTGTC	28
	MCH-ICG-1	: GGTGTGGACTTTGACTTCTGAATAG	29
	MCH-ICG-2	: CGGCAAAACGTGCGACTGTCA	30
55			

	MCH-ICG-3	: GGTGTGGTCCTTGACTTATGGATAG	210
	MGO-ICG-1	: AACACCCTCGGGTGCTGTCC	31
5	MGO-ICG-2	: GTATGCGTTGTCGTTTCGCGGC	32
	MGO-ICG-5	: CGTGAGGGGTCATCGTCTGTAG	33
	MUL-ICG-1	: GGTTTCGGGATGTTGTCCCACC	175
10	MGV-ICG-1	: CGACTGAGGTTCGACGTGGTGT	176
	MGV-ICG-2	: GGTGTTTGAGCATTGAATAGTGGTTGC	177
	MGV-ICG-3	: TCGGGCCGCGTGTTTCGTCAAA	211
15	MXE-ICG-1	: GTTGGGCAGCAGGCAGTAACC	178
	MSI-ICG-1	: CCGGCAACGGTTACGTGTTC	179
	MFO-ICG-1	: TCGTTGGATGGCCTCGCACCT	180
20	MFO-ICG-2	: ACTTGGCGTGGGATGCGGGAA	181
	MKA-ICG-5	: CCCTCAGGGATTTTCTGGGTGTTG	182
	MKA-ICG-6	: GGA CTCGTCCAAGAGTGTGTCC	183
25	MKA-ICG-7	: TCGGGCTTGGCCAGAGCTGTT	184
	MKA-ICG-8	: GGGTGCGCAACAGCAAGCGA	185
	MKA-ICG-9	: GATGCGTTGCCCCACGGG	186
30	MKA-ICG-10	: CCCTACGGGTAGCGTGTCTTTTG	187
	MML-ICG-1	: CGGATCGATTGAGTGCTTGTCC	188
	MML-ICG-2	: TCTAAATGAACGCACTGCCGATGG	189
35	MCE-ICG-1	: TGAGGGAGCCCGTGCTGTA	190
	MHP-ICG-1	: CATGTTGGGCTTGATCGGGTGC	191
	PA-ICG 1	: TGGTGTGCTGCGTGATCCGAT	34
40	PA-ICG 2	: TGAATGTTTCGTGGATGAACATTGATT	35
	PA-ICG 3	: CACTGGTGATCATTCAAGTCAAG	36
	PA-ICG 4	: TGAATGTTTCGT(G/A)(G/A)ATGAACATTGATTTCTGGTC	37
45	PA-ICG 5	: CTCTTTCACTGGTGATCATTCAAGTCAAG	38
	LIS-ICG 1	: CAAGTAACCGAGAATCATCTGAAAGTGAATC	39
	LMO-ICG 1	: AAACAACCTTTACTTCGTAGAAGTAAATTGGTTAAG	40
50	LMO-ICG 2	: TGAGAGGTTAGTACTTCTCAGTATGTTTGTTC	41
	LMO-ICG 3	: AGGCACTATGCTTGAAGCATCGC	42
	LIV-ICG 1	: GTTAGCATAAATAGGTAACATTTATGACACAAGTAAC	43
55	LSE-ICG 1	: AGTTAGCATAAGTAGTGTAACATTTATGACACAAG	44

	LISP-ICG 1	: CGTTTTTCATAAGCGATCGCACGTT	212
	CHTR-ICG 1	: GGAAGAAGCCTGAGAAGGTTTCTGAC	45
5	CHTR-ICG 2	: GCATTTATATGTAAGAGCAAGCATTCTATTCA	46
	CHTR-ICG 3	: GAGTAGCGTGGTGAGGACGAGA	47
	CHPS-ICG 1	: GGATAACTGTCTTAGGACGGTTTGAC	48
10	MPN-ICG 1	: ATCGGTGGTAAATTAAACCCAAATCCCTGT	49
	MPN-ICG 2	: CAGTTCTGAAAGAACATTTCCGCTTCTTTC	50
15	MGE-ICG 1	: CACCCATTAATTTTTTCGGTGTTAAAACCC	51
	Mycoplasma-ICG	: CAAAACCTGAAAACGACAATCTTTCTAGTTCC	52
	STAU-ICG 1	: TACCAAGCAAAACCGAGTGAATAAAGAGTT	53
20	STAU-ICG 2	: CAGAAGATGCGGAATAACGTGAC	54
	STAU-ICG 3	: AACGAAGCCGTATGTGAGCATTTGAC	55
	STAU-ICG 4	: GAACGTAACTTCATGTAAACGTTTGACTTAT	56
25	ACI-ICG 1	: GCTTAAGTGACAGTGCTCTAAACTGA	57
	ACI-ICG 2	: CACGGTAATTAGTGTGATCTGACGAAG	58
	BRU-ICG 1	: CGTGCCGCCTTCGTTTCTCTTT	59
30	BRU-ICG 2	: TTCGCTTCGGGGTGGATCTGTG	60
	BRU-ICG 3	: GCGTAGTAGCGTTTGCGTCGG	193
	BRU-ICG 4	: CGCAAGAAGCTTGCTCAAGCC	194
35	SALM-ICG 1	: CAAAACCTGACTTACGAGTCACGTTTGAG	61
	SALM-ICG 2	: GATGTATGCTTCGTTATTCCACGCC	62
	STY-ICG 1	: GGTCAAACCTCCAGGGACGCC	63
40	SED-ICG 1	: GCGGTAATGTGTGAAAGCGTTGCC	64
	YEC-ICG 1	: GGAAAAGGTACTGCACGTGACTG	198
	YEC-ICG 2	: GACAGCTGAAACTTATCCCTCCG	199
45	YEC-ICG 3	: GCTACCTGTTGATGTAATGAGTCAC	200
	CHTR-ICG 4	: GAGTAGCGCGGTGAGGACGAGA	201

50

55

Table 1b

	<u>PRIMERS</u>	<u>SEQUENCE</u>	<u>SEQ ID NO</u>
5	MYC-P1	: TCCCTTGTGGCCTGTGTG	65
	MYC-P2	: TCCTTCATCGGCTCTCGA	66
10	MYC-P3	: GATGCCAAGGCATCCACC	67
	MYC-P4	: CCTCCCACGTCCTTCATCG	68
	MYC-P5	: CCTGGGTTTGACATGCACAG	192
15	CHTR-P1	: AAGGTTTCTGACTAGGTTGGGC	69
	CHTR-P2	: GGTGAAGTGCTTGCATGGATCT	70
20	LIS-P1	: ACCTGTGAGTTTTTCGTTCTTCTC	71
	LIS-P2	: CTATTTGTTTCAGTTTTGAGAGGTT	72
25	LIS-P3	: ATTTTCCGTATCAGCGATGATAC	73
	LIS-P4	: ACGAAGTAAAGGTTGTTTTTCT	74
	LIS-P5	: GAGAGGTTACTCTCTTTTATGTCAG	75
30	LIS-P6	: CTTTATGTCAGATAAAGTATGCAA	202
	LIS-P7	: CGTAAAAGGGTATGATTATTG	203
35	BRU-P1	: TCGAGAATTGGAAAGAGGTC	204
	BRU-P2	: AAGAGGTCGGATTTATCCG	205
40	BRU-P3	: TTCGACTGCAAATGCTCG	206
	BRU-P4	: TCTTAAAGCCGCATTATGC	207
45	YEC-P1	: CCTAATGATATTGATTGCGG	208
	YEC-P2	: ATGACAGGTAAATCCTTACCCC	209

#### 50 **EXAMPLE 1: Pseudomonas aeruginosa**

55 **[0226]** Pseudomonas aeruginosa is a significant human pathogen, usually in the context of serious underlying disease. It is also a major cause of nosocomial infections, which are characteristically prone to resistance to antimicrobial agents. This gram-negative, non-fermentative rod can be responsible for different clinical manifestations, like wound infections, bacteremia, respiratory and urinary tract infections, and is also a major cause of morbidity and mortality in patients with cystic fibrosis.

**[0227]** Pseudomonas species are currently differentiated based on growth characteristics and several biochemical features implying a time schedule of 24h to 72h to get a correct identification of the pathogen.

[0228] Already the development of monoclonal or polyclonal antibodies significantly improved the identification of *Pseudomonas* species. Recently however it has been shown that it is possible to detect organisms directly in clinical samples on a very sensitive and specific way using DNA probes with or without a prior amplification of the target DNA.

[0229] DNA probes to study *Pseudomonas aeruginosa* are already described and are mainly used for epidemiological typing (Ogle et al., 1987; Samadpour et al., 1988; McIntosh et al., 1992). However, none of these probes have been derived from the 16S-23S spacer.

[0230] The 16S-23S rRNA gene spacer region and a part of the 23S rRNA gene was amplified with conserved primers (upper primer: TGGGGTGAAGTCGTAACAAGGTA, SEQ ID NO 155; lower primer: CCTTCCCTCACGGTACTGGT, SEQ ID NO 156) using the polymerase chain reaction for the following species :

- *Pseudomonas aeruginosa* 5669
- *Pseudomonas alcaligenes* LMG 1224<sup>T</sup>
- *Pseudomonas fluorescens* LMG 5167
- *Pseudomonas putida* LMG 2232
- *Pseudomonas stutzeri* LMG 2333<sup>T</sup>
- *Pseudomonas pseudoalcaligenes* LMG 1225<sup>T</sup>

[0231] To facilitate cloning of the obtained amplicons a *NotI* recognition site was added to the lower primer. After purification and digestion of the fragment with *NotI*, the amplicon was cloned in a *EcoRV/NotI* digested pBluescript SK<sup>+</sup> plasmid vector.

[0232] Sequencing of the 16S-23S rRNA gene spacer region was performed according the dideoxy-chain terminating chemistry either using double stranded plasmid DNA combined with primers located in the plasmid vector or directly on the PCR products after purification combined with internal PCR primers.

[0233] Fig. 36 to 40 represent the nucleotide sequence of the 16S-23S rRNA gene spacer regions from the different *Pseudomonas* species described above. For *P. fluorescens* only partial sequence information was obtained.

[0234] From the nucleic acid sequence of the spacer from *P. aeruginosa* strain 5669 five oligonucleotide-probes were chosen and chemically synthesized. The sequences of the oligonucleotides are the following :

PA1 = PA-ICG 1 : TGGTGTGCTGCGTGATCCGATA

PA2 = PA-ICG 2 : TGAATGTTCGTGGATGAACATTGATT

PA3 = PA-ICG 3 : CACTGGTGATCATTCAAGTCAAG

[0235] Specificity and sensitivity testing of the oligonucleotide-probes was carried out using a reverse hybridization assay. Genomic DNA of the different bacteria tested was amplified using biotinylated primers (idem primers as for cloning procedure, see above). The obtained amplicon, spanning the 16S-23S rRNA gene spacer region, was denatured and hybridized to a membrane-strip onto which the different oligonucleotide probes were immobilized in a line-wise fashion (LiPA). Hybridization was carried out in a mixture of 3xSSC (1xSSC = 0.15 M NaCl, 0.015 M sodium citrate, pH 7.0) and 20% formamide (FA) at a temperature of 50° C for one hour. Washing was done in the same mixture at the same temperature for 15 min.

[0236] Hybrids were detected using a streptavidine conjugate coupled to alkaline phosphatase and the probes were visualized through a precipitation reaction using NBT (nitrobluetetrazolium) and BCIP (bromo-chloro-indolylphosphate).

[0237] The hybridization results obtained with probes PA1, PA2 and PA3 are given in table 4 and show that probes PA1 and PA3 were 100% specific for *Pseudomonas aeruginosa* and hybridized to all the strains tested. The hybridization signal with probe PA3 at 50° C was not optimal, so the oligonucleotide-probe was improved by adding some additional nucleotides to the specific probe. This newly designed probe is PA5.

PA5 = PA-ICG 5 : CTCTTTCACCTGGTGATCATTCAAGTCAAG

[0238] Hybridization experiments with probe PA5 proved that this probe also shows a 100% specificity and 100% sensitivity for *P. aeruginosa*.

[0239] Oligonucleotide-probe PA2 hybridized only to 5 out of 17 *P. aeruginosa* strains tested. Direct sequencing of the 16S-23S rRNA gene spacer region of the strains which did not hybridize to these probes, showed some heterogeneity between different strains. Two mismatches were seen in comparison to the first developed PA2 probe. To

overcome this heterogeneity between different strains in the region of probe PA2 a new probe PA4 was designed. This probe is degenerated at the position of the mismatches and some additional nucleotides were added to improve the hybridization signal at 50° C.

PA4 = PA-ICG 4 : TGAATGTTCTGT(G/A)(G/A)ATGAACATTGATTTCTGGTC

[0240] A 100% specificity and 100% sensitivity was obtained with this degenerated probe as is shown by the hybridization results. i

Table 2 :

Hybridization results for <i>Pseudomonas</i>					
taxa tested	PA1	PA2	PA3	PA4	PA5
<i>Pseudomonas aeruginosa</i>	17/17	5/17	17/17	17/17	17/17
<i>Pseudomonas alcaligenes</i>	0/1	0/1	0/1	0/1	0/1
<i>Pseudomonas fluorescens</i>	0/1	0/1	0/1	0/1	0/1
<i>Pseudomonas putida</i>	0/1	0/1	0/1	0/1	0/1
<i>Pseudomonas pseudoalcaligenes</i>	0/1	0/1	0/1	0/1	0/1
<i>Pseudomonas stutzeri</i>	0/1	0/1	0/1	0/1	0/1
<i>Pseudomonas cepacia</i>	0/1	0/1	0/1	ND	ND
<i>Neisseria gonorrhoeae</i>	0/1	0/1	0/1	ND	ND
<i>Escherichia coli</i>	0/1	0/1	0/1	ND	ND
<i>Bordetella pertussis</i>	0/1	0/1	0/1	ND	ND
<i>Bordetella parapertussis</i>	0/1	0/1	0/1	ND	ND
<i>Bordetella bronchiseptica</i>	0/1	0/1	0/1	ND	ND
<i>Mycobacterium tuberculosis</i>	0/1	0/1	0/1	ND	ND
<i>Mycobacterium avium</i>	0/1	0/1	0/1	ND	ND
<i>Moraxella catarrhalis</i>	0/4	0/4	0/4	ND	ND
<i>Haemophilus influenzae</i>	0/2	0/2	0/2	ND	ND
<i>Streptococcus pneumoniae</i>	0/3	0/3	0/3	ND	ND
<i>Acinetobacter calcoaceticus</i>	0/1	0/1	0/1	ND	ND
<i>Staphylococcus aureus</i>	0/2	0/2	0/2	ND	ND
(n/m: number of strains positive/number of strains tested)					
(ND: not done)					

#### EXAMPLE 2: *Mycobacterium*

[0241] A variety of mycobacterial species may be involved in serious human infectious disease. Notorious examples are *Mycobacterium tuberculosis* and *Mycobacterium leprae*. Recently other species such as *M. avium*, *M. intracellulare* and *M. kansasii* have been more frequently encountered as human pathogens especially in immunocompromised hosts.

[0242] Consequently, laboratory diagnosis of mycobacterial infections should not be restricted to the *M. tuberculosis* complex but should ideally include most other clinically relevant mycobacterial species.

[0243] The identification and differentiation of pathogenic mycobacteria at the species level by conventional laboratory techniques is, in general, difficult and time-consuming.

[0244] To overcome these problems DNA-techniques were implemented. The techniques described extended from straightforward DNA-probing to automated sequence analysis. Several approaches have been recently reported (Jonas et al., 1993; Frothingham and Wilson, 1993; Tomioka et al., 1993; Saito et al., 1989; Vaneechoutte et al., 1993; Telenti et al., 1993; Boddington et al., 1990).

[0245] However, these methods all have their particular disadvantages, and most of them still rely on culture. Moreover, and most importantly, none of these techniques allows for a simultaneous detection of the different clinically relevant mycobacterial species in a single test run. Besides, the differentiation of particular groups within the *Mycobacterium avium-intracellulare* complex is problematic and often even impossible.

[0246] To overcome the above-mentioned disadvantages, a LiPA-test was developed which allows for the simulta-

neous and reliable detection and differentiation of a number of *Mycobacterium* species and groups. The sets of probes used to achieve these goals were all derived from the 16S-23S rRNA spacer region. The methods used are analogous to those mentioned in example 1.

[0247] The 16S-23S rRNA spacer region, and part of the 16S and 23S rRNA flanking genes, was amplified by PCR with primers conserved for the genus *Mycobacterium*. At least one of the following primers located in the 16S gene were used as upper primers:

MYC-P1: TCCCTTGTGGCCTGTGTG (SEQ ID NO 65)

MYC-P5: CCTGGGTTTGACATGCACAG (SEQ ID NO 192)

At least one of the following primers, located in the 23S gene, were used as lower primers for the amplification:

MYC-P2: TCCTTCATCGGCTCTCGA (SEQ ID NO 66)

MYC-P3: GATGCCAAGGCATCCACC (SEQ ID NO 67)

MYC-P4: CCTCCCACGTCCTTCATCG (SEQ ID NO 68)

All the above mentioned primers amplified the spacer region of all *Mycobacterium* strains tested, except primer MYC-P2 which was not functional for *M. chelonae*. In order to enhance the sensitivity of the detection, a nested PCR was sometimes carried out, using P5 and P4 as outer primers and P1 and P3 as inner primers.

[0248] In order to be able to design and select the probes and probe combinations which fit our purpose, the 16S-23S rRNA spacer region of a number of mycobacterial strains was sequenced. The obtained sequences were compared to each other and to those already known from literature (e.g. Frothingham et al., 1993, 1994; Kempell et al., 1992; Suzuki et al., 1988; EP-A-0395292; Van der Giessen et al., 1994; ) or from publicly accessible data banks. The corresponding sequences are represented in fig.1 to 35 (SEQ ID NO 76 to SEQ ID NO 110).

[0249] The probes derived from these data were all adjusted in such a way that the desired hybridization-behaviour was obtained using unified hybridization and wash conditions (i.e. 3xSSC, 20% deionized formamide, 50°C). The set of adjusted probes used for hybridization to different mycobacterial strains is represented in table 1a, SEQ ID NO 1-33. Please note that the probe nomenclature used in this example is an abbreviated version of the one used in table 1a: i.e. the letters "ICG" have always been omitted. According to the specific hybridization pattern obtained, the strains tested could be assigned to one of the following species or species groups: *M. tuberculosis* complex, *M. avium*, *M. intracellulare* or *M. intracellulare* complex, *M. kansasii*, *M. chelonae* and *M. goodii*. The strains tested which belong to each group are summarized in Table 4. All strains were obtained from the Institute of Tropical Medicine, Antwerp, Belgium. The different probe-patterns obtained for each group are illustrated in Table 3, and are discussed in more detail hereafter.

#### ***M. tuberculosis* complex**

[0250] The *M. tuberculosis* complex harbours all strains belonging to *M. tuberculosis*, *M. bovis*, *M. africanum* and *M. microti*. The probes **Mtb1**, **Mtb2** and **Mtb3** hybridize with DNA originating from all *M. tuberculosis* complex strains tested. None of the other strains tested hybridized with these probes at the conditions used.

[0251] In addition, *M. tuberculosis* complex strains, as is the case with all other mycobacterial strains tested, hybridize with either the **myc1** or the **myc22** probe or both. The latter two probes are designed as general *Mycobacterium* probes, either alone or in combination with each other.

#### ***M. avium*/*M. paratuberculosis***

[0252] All *M. avium* and *M. paratuberculosis* strains studied reveal an identical hybridization pattern with the set of probes. For this type of organisms positive hybridization signals are obtained with the probes **myc1/myc22**, **mail**, **milli**, **mav1**, **mah1** and **mav22**. The latter two probes hybridize exclusively with *M. avium* and *M. paratuberculosis* strains, and can thus be used as species-specific probes. Since the 16S-23S spacer sequences of *M. avium* isolates and *M. paratuberculosis* isolates are identical or nearly identical these two taxa cannot be discriminated from each other. This finding supports 16S rRNA sequencing data which indicate that *M. avium* and *M. paratuberculosis* should in fact be considered as belonging to one geno-species (Rogal et al., 1990), *M. avium* ssp. *avium* and *M. avium* ssp. *paratuber-*



culosis.

#### **M. intracellulare and M. intracellulare complex (MIC)**

5 [0253] MIC strains are genotypically highly related organisms, which, according to sequence data of the 16S-23S rRNA spacer region, belong to a distinct cluster which is separate from other *Mycobacterium* species. *M. avium* and *M. scrofulaceum* are their closest relatives. Almost all strains tested which are generally referred to as *M. avium* complex (MAC) strains (the former MAIS-complex) can be found in the MIC group. Thus, the MIC group defined in the current invention encompasses the MAC-type strains described by Frothingham and Wilson (1993) with the exception of MAC-G which appears to be *M. scrofulaceum*. Also *M. intracellulare* strains *sensu stricto* (*M. intracellulare* s.s.) are part of this cluster.

[0254] Because this MIC group contains a quite large group of strains with, among them, subgroups showing different hybridization characteristics to the set of probes, a further subdivision into MIC-types was envisaged.

15 [0255] Type MIC 1 harbours *M. intracellulare* s.s., together with some other MAC-strains. All MIC 1 type isolates, without exception, hybridize to the following probes: myc1/myc22, mail and macl. The following probes can be used to make further subdivisions within the MIC 1 group: mil11, min1, min2 to 2222, mil22 and mhef1.

[0256] *M. intracellulare sensu stricto* strains (type MIC 1.1.a) can be distinguished from other subtypes in this group by virtue of probe min1 which is positive only for this group of strains. All strains of type MIC 1.1.a strains are positive when tested with the *M. intracellulare* probe of the Gen-Probe Rapid Diagnostic system for MAC.

20 [0257] Type MIC 1.1.b and MIC 1.2 harbour strains which are highly related to *M. intracellulare*. They can be differentiated by using probes mil11 and mil22 (see Table 3). Further subdivision within these groups was not attempted although this could be achieved by using the probes: mln2, mln22, mln222 and mln2222. Further subdivision might be of value for epidemiological reasons.

25 [0258] Only two of our collection of strains tested group as MIC 2 strains. One of these strains is a "*Mycobacterium lufu*" strain (ITG 4755). The specific probe pattern generated by these strains is characterized by a positive hybridization signal with the following probes: myc1/myc22, mail, mil22, mah1 and mal1. Variable hybridization results are obtained with probes min2222, mac1 and mhef1. The other probes are negative. It is not unlikely that MIC 2 would eventually prove to be a heterogeneous group when more strains of this type are being identified. The variable probes may help in a further differentiation, if this would become relevant.

30 [0259] Type MIC 3 groups a fairly high number of MAC-strains which are rather remotely related to *M. intracellulare* s.s. strains and most other MAC-strains. This cluster should be regarded as distinct from *M. avium* and *M. intracellulare* on genotypical grounds. All

[0260] MIC 3 subtypes hybridize to probes myc1/myc22, mail, mil22 and mcol. A positive signal with the latter probe (mcol) is characteristic for MIC 3 strains. Variable hybridization results are obtained with the following probes: mac1 mhef1 and mah1.

35 [0261] MIC 3 can be further subdivided into four subtypes by using three probes: mthll, mth2 and mef11. Probe mth2 is specific for type MIC 3.1 which encompasses a group of highly related MAC-strains isolated from immunocompromised human beings.

40 [0262] Most MIC 3 strains are located in the MIC 3.1 subtype. Eventually species status may be assigned to this group of strains, as might also be the case for other groups of MAC strains, yet unnamed. In subtypes MIC 3.4, MIC 3.3 and MIC 3.2 only two, one and one strain are found respectively in our collection of strains tested.

45 [0263] Type MIC 4 is a collection of "MAIS" strains (including *M. malmoense*) which are remotely related to *M. intracellulare*. The only probe of the above-described set which hybridizes to MIC 4, apart from the general myc1/myc22 probes, is the mail probe. This probe shows a broad specificity, hybridizing also with *M. avium*, *M. intracellulare* and other MIC strains and *M. scrofulaceum*.

#### **M. scrofulaceum**

50 [0264] All *M. scrofulaceum* strains tested reveal an identical hybridization pattern with the set of probes. A positive signal with probe msc1 is unique to *M. scrofulaceum* strains. The only other probes with a positive signal for this species are evidently myc1/myc22 and also mail.

#### **M. kansasii**

55 [0265] Probes mka3 and mka4 are specific for *M. kansasii*; i.e. a distinct positive signal is obtained on the LiPA strip when amplified DNA from the *M. kansasii* strains is used in the hybridization whilst with all other organisms tested the signal is absent. Although the sequences of probes mka1 and mka2 are not absolutely complementary to the target sequence (3 and 1 mismatches, respectively), these probes also proved to be useful since they hybridized exclusively

to *M. kansasii* DNA and not to any other mycobacterial DNA tested under the conditions used (50°C, 3xSSC, 20% formamide). This illustrates that probes not necessarily have to match perfectly to the target to be useful, and that modifications in sequence and length may be allowed up to a certain degree.

#### 5 *M. chelonae*

[0266] The species *M. chelonae* encompasses *M. chelonae* ssp. *chelonae* and *M. chelonae* ssp. *abscessus* strains. The spacer region was sequenced for one strain of each subspecies and small differences were noticed (SEQ ID NO 103 and SEQ ID NO 102). Probes **mch1** and **mch2** hybridize to both strains. All other probes are negative for these  
10 2 strains except for **mycl/myc22**.

[0267] Upon testing of probes **mch1** and **mch2** with 2 additional *M. chelonae* strains not mentioned in table 4, i.e. *M. chelonae* 94-379 and *M. chelonae* 94-330, both obtained from the Institute of Tropical Medicine in Antwerp, Belgium, it appeared that they did not hybridize to probe **mch1**. This was confirmed by sequencing the spacer region of these two strains (SEQ ID NO 184). Cluster analysis of the spacer region with other mycobacteria revealed that *M. chelonae*  
15 strains can be subdivided in two groups. A third probe **mch3** was designed to specifically detect this second group of strains, to which 94-379 and 94-330 belong.

[0268] This illustrates that the use of DNA probes derived from the 16S-23S rRNA spacer region can be helpful in differentiating different groups of strains, which belong to the same species according to the classical identification methods, and possibly can be used to detect and describe new species within the mycobacteria. In this case **mch2**  
20 detects all *M. chelonae* strains, whereas **mch1** and **mch3** differentiate between different subgroups.

#### *M. gordonae*

[0269] The five *M. gordonae* strains tested all hybridize to probe **mgo5**. Positive hybridization signals are also ob-  
25 tained with probes **mycl/myc22**, and some *M. gordonae* strains also hybridize to probes **mgol** and **mgo2**.

#### other mycobacterial species

[0270] Strains belonging to other mycobacterial species than those mentioned above only hybridize to the general  
30 probes **myc1/myc22**. This indicates that these strains most probably belong to the genus *Mycobacterium*, but do not belong to one of the species or groups which can be specifically identified by using one or more of the other probes described.

[0271] In conclusion we can state that, according to the particular combinations of probes of the invention used, DNA probe tests at different levels can be provided.

[0272] When all probes are used in one and the same LiPA-test, differentiation at the species level as well as sub-  
35 typing of certain groups of mycobacteria can be achieved. However, the probe-assembly on one strip could be restricted to those probes which are species-specific; in that case identification is performed at the species level. A further reduction of the number of probes on the strip might lead to the specific detection of only one or just a few species. Obviously, LiPA strips can be designed which solely attempt to subtype strains, e.g. those belonging to the *M. intrac-*  
40 *ellulare* complex (MIC). Depending on the particular needs of the laboratoria performing diagnosis and/or typing of mycobacteria, all these different applications might be of value. However, it is clear that by using a combination of probes in a LiPA-format the amount of information obtained as to the identity of the organisms present in the clinical sample, is considerably increased as compared to DNA probe tests using only a single probe. For some groups, or at  
45 least for further subdivision of some groups, a single probe uniquely hybridizing to this (sub)group could not be designed. In that case only probe-patterns are able to provide the information needed. For these applications the LiPA is an advantageous format.

Table 3 : Different probe patterns obtained for mycobacterial (sub)species

Mycobacterium	myc1 myc22	mtb1 mtb2 mtb3	maif	mil11	mav1 mav22	min1	min222	min22	min2	min2222	mil22	mac1
M. tuberculosis	+	+	-	-	-	-	-	-	-	-	-	-
M. bovis					+	-	-	-	-	-	-	-
M. avium	+	-	+	+		-	-	-	-	-	-	-
M. paratuberculosis												
MIC 1.1.a	+	-	+	+	-	+	+	+	+	+	+	+
MIC 1.1.b	+	-	+	+	-	-	-	-	-	-	-	+
MIC 1.2	+	-	+	+	-	-	-	-	-	-	-	+
MIC 2	+	-	+	-	-	-	-	-	-	-	-	+
MIC 3.4	+	-	+	-	-	-	-	-	-	-	-	+
MIC 3.3	+	-	+	-	-	-	-	-	-	-	-	+
MIC 3.1	+	-	+	-	-	-	-	-	-	-	-	+
MIC 3.2	+	-	+	-	-	-	-	-	-	-	-	+
MIC 4	+	-	+	-	-	-	-	-	-	-	-	-
M. scrofulaceum	+	-	+	-	-	-	-	-	-	-	-	-
M. kansasii	+	-	+	-	-	-	-	-	-	-	-	-
M. chelonae	+	-	+	-	-	-	-	-	-	-	-	-
M. goodii	+	-	+	-	-	-	-	-	-	-	-	-
Mycobacterium sp.	+	-	+	-	-	-	-	-	-	-	-	-

**Table 3: continued**

Mycobacterium	mco1	mtbh1	mtbh2	mefl1	mhefl	mah1	mali	mssl	mka1,2,3,4	meh 1,2,3	mgol,2	ngo5
M. tuberculosis M. bovis	-	-	-	-	-	-	-	-	-	-	-	-
M. avium M. paratuberculosis	-	-	-	-	-	+	-	-	-	-	-	-
MIC I.1.a MIC I.1.b MIC I.2	- - -	- - -	- - -	- - -	- - +	- - +	- - -	- - -	- - -	- - -	- - -	- - -
MIC 2	-	-	-	-	+/-	+	+	-	-	-	-	-
MIC 3.4 MIC 3.3 MIC 3.1 MIC 3.2	+ + + +	- + + -	- - + -	+ + - -	+ + +/= +	+ + + +	- - - w	- - - -	- - - -	- - - -	- - - -	- - - -
MIC 4	-	-	-	-	-	-	-	-	-	-	-	-
M. scrofulaceum	-	-	-	-	-	-	-	+	-	-	-	-
M. kansasii M. chelonae M. goodii Mycobacterium sp.	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -	++ - - -	- $\pm$ - -	- - + -	- - + -

w : weak / v : very weak / + : + or -, variable according to the strain tested

Table 4

Mycobacteria strains tested in LIPA	
species/group	strain numbers from Institute of Tropical Medicine Antwerp (except those between parentheses)
M. tuberculosis complex	7602, 8004, 8017, 8647, 8872, 9081, 9129, 9173, 9517, (ATCC 27294), 8324, 8428
M. avium/ M. paratuberculosis	1101, 1983, 2070, 2074, 4176, 4189, 4191, 4193, 4197, 4204, 4386, 4991, 5872, 5874, 5884, 5887, 5893, 5894, 5897, 5903, 5904, 5905, 5927, 5983, 8180, 8750, (ATCC 25291), <u>M. paratub</u> : (316F), (2E)
M. intracellulare (MIC 1.1.a)	4199, 4208, 5701, 5880, 5906, 5908, 5909, 5913, 5915, 5917, 5918, 5920, 5921, 5924, 5925, 5929, 8713, 8717, 8718, 8720, 8721, 8722, 8732, 8740, 8741, 8742, 8744, 8747, 8749
MIC 1.1.b	8694, 8745, 8754 8708 5513, 8743 8054, 8190
MIC 1.2	8710, 8711, 8712, 8714, 8715, 8716, 8725, 8729, 8733, 8737, 8746, 8751, 8752 5919 8695 8748
MIC 2	5922 4755 (M. lufu)
MIC 3.4	1815 8707
MIC 3.3	5620
MIC 3.1	925, 926, 1329, 1788, 1794, 1812, 1818, 2069, 2073, 2076, 4541, 4543, 5074, 5280, 5789, 7395, 8739, 8753 8738
MIC 3.2	5765
M. scrofulaceum	4979, 4988, 5907, 8706, 8726, 8727, 8735, (MB022), (MB023), (MB024)
M. kansasii	4987, (ATCC 22478)
M. chelonae	4975, 9855
M. goodii	7703, 7704, 7836, 7838, 8059
MIC 4	8723, 8724 8757 4842 (M. malmoense)
other mycobacterial species	7732 (M. marinum), 94-123 (M. celatum), 778 (M. haemophilum), 8777 (M. genavense), 4484 (M. siniae), 4986 (M. xenopi), 4304 (M. fortuitum), 1837 (M. ulcerans)

**EXAMPLE 3: Listeria**

[0273] Listeria species are a group of Gram-positive rods widely spread in nature. Within this group it seems that only L. monocytogenes is pathogenic to humans and animals. L. monocytogenes is the causative agent of listeriosis, giving rise to meningitis, abortions, encephalitis and septicemia. Immunocompromised individuals, newborn infants

and pregnant women are high risk groups for this foodborne disease. Most cases have been caused by the consumption of food of animal origin, particularly soft cheeses. Therefore, the presence of *L. monocytogenes* should be excluded from food. For safety measurements, in some countries, the absence of all *Listeria* species is required in food products.

[0274] The classical identification method for *L. monocytogenes* in dairy products involves an enrichment culture for 48 h and subsequently colony forming on selective agar medium for 48 h followed by a whole set of biochemical and morphological assays (Farber and Peterkin, 1991). This procedure could be very much simplified by the use of gene probes.

[0275] Several DNA probes are already described for the identification of *L. monocytogenes*. Some probes are derived from genes responsible for the pathogenicity of the organism, for instance the listeriolysin O gene (Datta et al., 1993) or the invasion-associated-protein (iap) (Bubert et al., 1992).

[0276] A commercially available identification system, based on a specific 16S rRNA probe, was introduced by Gen-Probe (Herman and De Ridder, 1993; Ninet et al., 1992).

[0277] These specific probes are used as confirmation assays on colonies obtained after enrichment and plating on selective agar medium.

[0278] Recently several publications reported on the use of the polymerase chain reaction to amplify the target region for the DNA probes, which can shorten the time of the assay without interfering with the specificity and the sensitivity of the assay. Different primer sets are described that can specifically amplify *L. monocytogenes* DNA. These primer sets were derived from the listeriolysin O gene (Golstein Thomas et al., 1991), and the iap gene (Jaton et al., 1992).

[0279] We used the 16S-23S rRNA gene spacer region as the target for the development of a genus-specific probe for *Listeria* and a probe specific for *Listeria monocytogenes*.

[0280] Using conserved primers derived from the 3' end of the 16S rRNA and the 5' end of the 23S rRNA (sequences are given in example 1) the spacer region was amplified using the polymerase chain reaction and subsequently cloned in a suitable plasmid vector following the same procedures as in example 3.

[0281] Two amplicons differing in length (800 bp and 1100 bp) were obtained. Both PCR fragments were cloned for the following *Listeria* species:

- *Listeria monocytogenes*, serovar 4b, IHE (Instituut voor Hygiëne en Epidemiologie, Belgium)
- *Listeria ivanovii* CIP 78.42 (Collection Nationale de Cultures de Microorganismes de l'Institut Pasteur, France)
- *Listeria seeligeri* serovar 4a, nr. 42.68 (Bakteriologisches Institut, Südd, Versuchs- und Forschungsanstalt für Milchwirtschaft Weihenstephan, Germany)

[0282] The sequence of the spacer region between the 16S and 23S rRNA gene was determined using the cloned material originating from the 800 bp PCR fragment and this was done for the three described *Listeria* species. Fig. 41 to 43 show the sequences of the different short spacer regions obtained. The sequence of this short spacer region of *L. monocytogenes* was also retrieved from the EMBL databank (LMRGSPCR).

[0283] Based on this sequence information, following oligonucleotides for species-specific detection were chosen and chemically synthesized :

LMO-ICG-1 : AAACAACCTTTACTTCGTAGAAGTAAATTGGTTAAG

LMO-ICG-2 : TGAGAGGTTAGTACTTCTCAGTATGTTTGTTT

LSE-ICG-1 : AGTTAGCATAAGTAGTGTAAGTATTTATGACACAAG

LIV-ICG-1 : GTTAGCATAAATAGGTAAGTATTTATGACACAAGTAAC

Also, a genus specific probe for *Listeria* was designed:

LIS-ICG-1 : CAAGTAACCGAGAATCATCTGAAAGTGAATC

The oligonucleotide-probes were immobilized on a membrane strip and following reverse hybridization with biotinylated PCR fragments, the hybrids were visualized using a precipitation reaction. The hybridization results of different *Listeria* species are summarized in table 5.

Table 5

Species	n	LIS1	LMO1	LMO2	LSE1 1	LIV1
<i>L. monocytogenes</i>	1	+	+	+	-	-
<i>L. seeligeri</i>	2	+	+	±	-	±
<i>L. ivanovii</i>	3	+	±	-	±	+
<i>L. welshimeri</i>	3	+	+	±	-	-
<i>L. innocua</i>	2	+	+	+	-	-

[0284] These hybridization results show that probe LIS1 can detect all described *Listeria* species, but also that the species-specific probes cross-hybridize to each other. Hence, from this short spacer region probes with sufficient specificity could not be found.

[0285] For *Listeria monocytogenes* the 16S-23S rRNA gene spacer was also determined originating from the 1100 bp fragment. Fig. 45 shows the sequence obtained for this species. This sequence information was also obtained for *L. seeligeri* (see fig. 46) and partial sequence information of the large spacer region was obtained for *L. ivanovii* (see fig. 44).

[0286] Based on sequence alignment with *L. seeligeri* following oligonucleotide-probe was chosen to specifically detect *L. monocytogenes*.

LMO-ICG-3 : AGGCACTATGCTTGAAGCATCGC

[0287] Initial hybridization results (not shown) indicated that no cross-hybridization with other *Listeria* species was seen with this *L. monocytogenes* probe LMO3, and that all *Listeria* strains used hybridized to the general probe LIS 1.

[0288] The oligonucleotide-probes, LIS1 for detection of all *Listeria* species and LMO3 for specific detection of *L. monocytogenes*, were immobilized on a membrane strip and hybridized to labeled amplicons, containing the 16S-23S rRNA spacer region, derived from different organisms. The hybridization results are shown in the following table.

[0289] An excellent specificity and sensitivity were obtained for probes LMO3 and LIST respectively at the species and genus level.

Table 6

Taxa tested	n	LIS1	LMO3
<i>Listeria monocytogenes</i>	44	+	+
<i>Listeria ivanovii</i>	10	+	-
<i>Listeria seeligeri</i>	11	+	-
<i>Listeria welshimeri</i>	16	+	-
<i>Listeria innocua</i>	23	+	-
<i>Listeria murrayi</i>	3	+	-
<i>Listeria grayi</i>	2	+	-
<i>Brochotrix thermosphacta</i>	1	-	-
<i>Brochotrix campestris</i>	1	-	-
<i>Bacillus cereus</i>	3	-	-
<i>Bacillus brevis</i>	2	-	-
<i>Bacillus coagulans</i>	1	-	-
<i>Bacillus pumilis</i>	1	-	-
<i>Bacillus macerans</i>	1	-	-
<i>Bacillus lentus</i>	1	-	-
<i>Bacillus firmus</i>	2	-	-
<i>Bacillus subtilis</i>	2	-	-
<i>Bacillus megaterium</i>	1	-	-
<i>Enterococcus faecalis</i>	1	-	-
<i>Enterococcus faecium</i>	1	-	-

Table 6 (continued)

Taxa tested	n	LIS1	LMO3
<u>Enterococcus durans</u>	1	-	-
<u>Lactococcus lactis</u>	3	-	-
<u>Lactococcus casei</u>	1	-	-
<u>Escherichia coli</u>	1	-	-
<u>Hafnia halvei</u>	1	-	-
<u>Agrobacterium tumefaciens</u>	2	-	-
<u>Mycoplasma dimorpha</u>	1	-	-
<u>Clostridium tyrobutyricum</u>	1	-	-
<u>Clostridium perfringens</u>	1	-	-
<u>Clostridium sporogenes</u>	1	-	-
<u>Clostridium acetobutyricum</u>	1	-	-
<u>Brucella abortus</u>	1	-	-
<u>Brucella suis</u>	1	-	-
<u>Brucella melitensis</u>	1	-	-
<u>Staphylococcus aureus</u>	1	-	-
<u>Salmonella typhimurium</u>	1	-	-
<u>Salmonella enteritidis</u>	1	-	-
<u>Yersinia enterocolitica</u>	1	-	-
n: number of strains tested			

[0290] These two probes can be used for the detection of Listeria species and Listeria monocytogenes directly on food samples or after enrichment of the samples in liquid broth. In both cases amplification problems can occur with the conserved primers due to the enormous background flora in these samples.

[0291] To circumvent this problem, we designed several sets of primers derived from the 16S-23S rRNA spacer regions of Listeria species.

[0292] Primers LIS-P1 and LIS-P2 are upper primers, whereas LIS-P3 and LIS-P4 are lower primers. These primers amplify the smaller 16S-23S rRNA spacer region as well as the larger spacer of Listeria species (except L. grayi and L. murrayi). If needed these primers can be used in a nested PCR assay where LIS-P1/LIS-P4 are the outer primers and LIS-P2/LIS-P3 are the inner primers.

[0293] For the specific detection of Listeria monocytogenes probe LMO-ICG-3 was designed and derived from the large 16S-23S rRNA spacer region. In order to specifically amplify only this large spacer region for an improved detection of this pathogen directly in samples a set of primers was derived from the part of sequence information from the large 16S-23S rRNA spacer region that is not present in the smaller rRNA spacer. For this aim, primers LIS-P5 and LIS-P6 are used as the upper primers and LIS-P7 is used as the lower primer.

LIS-P1 : ACCTGTGAGTTTTCGTTCTTCTC 71

LIS-P2 : CTATTTGTTTCAGTTTTCGAGAGGTT 72

LIS-P3 : ATTTTCCGTATCAGCGATGATAC 73

LIS-P4 : ACGAAGTAAAGGTTGTTTTTCT 74

LIS-P5 : GAGAGGTTACTCTCTTTTATGTCAG 75

LIS-P6 : CTTTATGTCAGATAAAGTATGCAA 202

LIS-P7 : CGTAAAAGGGTATGATTATTTG 203

[0294] During the evaluation of the probes for Listeria spp. an organism was isolated from cheese that resembled Listeria according to the classical determination methods. This isolate (MB 405) showed the following characteristics (similar to Listeria spp.): Gram positive, growth on Oxford and Tryptic Soy Agar, catalase positive. The only difference with the Listeria spp. was the motility, which was negative.



[0295] Using the conserved primers as described in example 1 in order to amplify the 16S-23S rRNA spacer region of this isolate MB 405, the same amplicon pattern was obtained with this strain as with *Listeria* spp. Hybridization of the amplicon showed that there was no signal obtained with any of the probes for *Listeria* spp.

[0296] Sequencing of the 16S rRNA of isolate MB 405 and subsequent comparison with *Listeria* spp. and relatives showed that the organism was more closely related to *Listeria* spp. than to any other species described in the literature until now. Taxonomical studies will show if this isolate does or does not belong to the genus *Listeria*. This isolate, and subsequently isolated organisms from the same type, are referred to in this application as *Listeria* like organisms.

[0297] Isolate MB 405 seemed to contain at least 3 different 16S-23S rRNA spacer regions which were cloned and sequenced. Following alignment with *Listeria* spp. an oligonucleotide-probe was chosen to specifically detect *Listeria*-like strains:

LISP-ICG-1 : CGTTTTCATAAGCGATCGCACGTT

Reverse hybridization reactions of this probe with the 16S-23S rRNA spacer regions of *Listeria* spp. showed that there was no cross-hybridization.

#### EXAMPLE 4: *Chlamydia trachomatis*

[0298] *Chlamydia trachomatis* is a small obligate intracellular gram-negative bacterium, which has 15 serovars (A-K, Ba, L1, L2, and L3) distinguished by the major outer membrane protein (MOMP) and contains a cryptic plasmid required for intracellular growth. The A-K and Ba serovars constitute the trachoma biovar, while the L1, L2, and L3 serovars constitute the LGV biovar.

[0299] Serovars A, B, Ba, and C are commonly associated with trachoma, the leading cause of preventable blindness worldwide. The D-K serovars are found mainly in sexually transmitted infections and are the major cause of cervicitis and pelvic inflammatory disease in women, and urethritis and epididymitis in men. Serovars L1, L2 and L3 are involved in lymphogranuloma venereum, a rare sexually transmitted disease.

[0300] Cell culture is regarded as the benchmark method for laboratory diagnosis, although specimen viability is difficult to maintain during transport and laboratory techniques are time-consuming and technically demanding. Therefore, a number of more rapid test kits were developed, such as an enzyme-linked immunosorbent assay, and direct fluorescent-antibody staining. However, none of these immunoassays have been shown to have high levels of sensitivity or specificity.

[0301] A nonisotopic DNA probe assay (Gen-Probe PACE; Woods et al., 1990) that detects chlamydial rRNA is commercially available. Recently, the polymerase chain reaction (PCR) method has been used for detection of *Chlamydia* infections. Detection was targeted at either the cryptic plasmid (Loeffelholz et al., 1992), or the *omp1* gene, which encodes for the major outer membrane protein (Taylor-Robinson et al., 1992). Compared with other techniques, PCR has higher sensitivity and specificity (Ossewaarde et al., 1992). None of these assays make use of DNA probes derived from the 16S-23S rRNA gene spacer region.

[0302] For a *Chlamydia trachomatis* L2 and a *Chlamydia psittaci* 6BC strain, a part of the ribosomal RNA cistron, containing the 16S-23S rRNA spacer region was amplified using conserved primers (see example 1) and subsequently cloned in a plasmid vector. The 16S-23S rRNA spacer region was sequenced using the dideoxychain terminating chemistry.

[0303] The sequence of the spacer region of both *Chlamydia* species is shown in fig. 47 to 48.

[0304] Based on this sequence information, following oligonucleotide-probes were chemically synthesized :

CHTR-ICG-1 : GGAAGAAGCCTGAGAAGGTTTCTGAC

CHTR-ICG-2 : GCATTTATATGTAAGAGCAAGCATTCTATTTC

CHTR-ICG-3 : GAGTAGCGTGGTGAGGACGAGA

CHPS-ICG-1 : GGATAACTGTCTTAGGACGGTTTGAC

[0305] The oligonucleotide-probes were immobilized in a line-wise fashion on a membrane strip and subsequently used in a reverse hybridization assay with biotinylated PCR products, containing the 16S-23S rRNA spacer region, as target.

[0306] Hybridizations were done in a solution of 3xSSC and 20% formamide (FA) at a temperature of 50°C.

[0307] The hybridization results with the different probes are shown in the following table.

Table 7

Strains tested	CHTR1	CHTR2	CHTR3	CHPS1
<u>Chlamydia trachomatis</u> L2	+	+	+	-
<u>Chlamydia psittaci</u> 6BC	-	-	-	+
<u>Chlamydia psittaci</u> CP	-	-	-	+
<u>Chlamydia psittaci</u> TT	-	-	-	+
<u>Haemophilus ducreyi</u> CIP 542	-	-	-	-
<u>Haemophilus influenzae</u> NCTC 8143	-	-	-	-
<u>Neisseria gonorrhoeae</u> NCTC 8375	-	-	-	-
<u>Moraxella catarrhalis</u> LMG 5128	-	-	-	-
<u>Escherichia coli</u> B	-	-	-	-
<u>Streptococcus pneumoniae</u> S92-2102	-	-	-	-

[0308] As shown in the table at a hybridization temperature of 50°C the probes CHTR1, CHTR2 and CHTR3 are specific for Chlamydia trachomatis and probe CHPS1 is specific for Chlamydia psittaci.

[0309] Several clinical isolates, obtained from the SSDZ, Delft, Netherlands, identified as Chlamydia trachomatis using conventional methods were tested in a reverse hybridization assay with the different oligonucleotide-probes. All Chlamydia trachomatis specific probes gave a positive hybridization signal and none of the isolates reacted with the Chlamydia psittaci probe. For some clinical isolates the CHTR2 probe reacted significantly weaker than CHTR1 or CHTR3. The spacer region of one of these isolates (94 M 1961) was sequenced (SEQ ID NO 197) and the sequence revealed one mismatch with the spacer sequence of strain L2. An additional probe (CHTR4) was derived from this new spacer sequence:

CHTR-ICG-4 : GAGTAGCGCGGTGAGGACGAGA

(SEQ ID NO 201)

This probe gives a stronger hybridization signal than CHTR2 with some clinical isolates from Chlamydia trachomatis. It can be used alone, or in combination with the CHTR2 probe (e.g. both probes applied in one LiPA-line).

[0310] In order to develop very sensitive assays for the detection of Chlamydia trachomatis directly in clinical specimens a specific primer set was derived from the 16S-23S rRNA spacer region, CHTR-P1 (upper primer) and CHTR-P2 (lower primer), amplifying specifically the spacer region of Chlamydia species.

CHTR-P1 : AAGGTTTCTGACTAGGTTGGGC

69

CHTR-P2 : GGTGAAGTGCTTGCATGGATCT

70

#### EXAMPLE 6: Mycoplasma pneumoniae and Mycoplasma genitalium

[0311] Mycoplasmas are a group of the smallest prokaryotes known that are able to grow in cell-free media, lack a cell wall, and have very small genomes with a low G+C content. More than 100 different species have been isolated from humans, animals, plants, and insects.

[0312] In humans, mycoplasmas have been recognized either as pathogenic organisms or as commensals. The best known pathogen is Mycoplasma pneumoniae, the causative agent of primary atypical pneumonia, especially in children and young adults. The diagnosis of M. pneumoniae has been based on the direct isolation by the culture method or on the detection of specific antibodies against M. pneumoniae in the patient's serum.

[0313] Another pathogen, first isolated from urethral specimens from patients with nongonococcal urethritis, has been described as Mycoplasma genitalium. This mycoplasma has several properties in common with M. pneumoniae. Both species are pathogenic, and both possess the capability to adhere to erythrocytes, various tissue cells, glass, and plastic surfaces. Furthermore, M. genitalium and M. pneumoniae share antigens, giving rise to extensive cross-reactions in serological tests. The observation that M. genitalium could also be found in respiratory tract specimens from patients with pneumonia and isolated from a mixture with M. pneumoniae has raised questions to the possible pathogenicity of M. genitalium.

[0314] Since cultivation of both species is time-consuming and serology lacks specificity, more rapid and more specific assays were developed to identify these mycoplasmas. The use of hybridization assays with DNA probes was described for these species, but despite good specificities these tests do not allow the detection of low levels of *M. pneumoniae* or *M. genitalium*. So more recently, DNA hybridization techniques were developed using the polymerase chain reaction. *M. pneumoniae*-specific PCR assays have been reported using the P1 adhesin gene (Buck et al., 1992) and the 16S rRNA gene (Kuppeveld et al., 1992). Specific PCR assays for *M. genitalium* were described using sequences from the adhesin gene and the 16S rRNA gene.

[0315] The spacer sequences of clinical isolates of *M. pneumoniae* and *M. genitalium* (obtained from U. Gobel, University of Freiburg, Germany) were determined. They are shown in fig. 49 to 50. The sequences show some differences to those from other strains of the same species deposited in the EMBL databank (MPMAC and MGG37 respectively). Based on this information four probes were derived: one general Mycoplasma probe, two *M. pneumoniae* specific, and one *M. genitalium* specific probe:

Mycoplasma-ICG: CAAAACTGAAAACGACAATCTTTCTAGTTCC

MPN-ICG-1: ATCGGTGGTAAATTAAACCCAAATCCCTGT

MPN-ICG-2: CAGTTCTGAAAGAACATTTCCGCTTCTTTC

MGE-ICG-1: CACCCATTAATTTTTTCGGTGTTAAAACCC

[0316] The probes were applied to LiPA strips and hybridized under standard conditions (3X SSC, 20% formamide at 50°C) to amplified spacer material from four *M. pneumoniae* strains, one *M. genitalium* strain and twenty-two non-Mycoplasma species strains. The general probe hybridized only to the five *Mycoplasma* strains tested, while the specific probes hybridized only to strains of the species for which they were designed.

#### EXAMPLE 7: Other mycobacterial species

[0317] With the steady improvement of laboratory techniques the information on the systematics and clinical significance of the so called "potentially pathogenic environmental mycobacteria" increased rapidly. With the emergence of newly recognized diseases, additional syndromes associated with different mycobacterial species have emerged and have assumed major importance.

[0318] In order to extend the LiPA test for the simultaneous detection of different mycobacterial species as described in example 2, a new set of DNA probes was designed to specifically identify the following species: *Mycobacterium ulcerans*, *Mycobacterium genavense*, *Mycobacterium xenopi*, *Mycobacterium simiae*, *Mycobacterium fortuitum*, *Mycobacterium malmoeense*, *Mycobacterium celatum* and *Mycobacterium haemophilum*.

[0319] These probes were derived from the 16S-23S rRNA spacer region sequence. For the above mentioned species this information was obtained through direct sequencing of PCR products or after cloning of the PCR-amplified spacer region. The sequences obtained are represented in fig. 80 to 97, and in fig. 38 for *M. malmoeense*.

[0320] The sequences of the spacer region of the above-mentioned mycobacterial species were compared and aligned to those already described in example 2 or in publicly available sources. From the regions of divergence, species-specific DNA probes were designed. The probes were selected and designed in such a way that the desired hybridization behaviour (i.e. species-specific hybridization) was obtained under the same conditions as those specified for the other mycobacterial probes mentioned in example 2, i.e. 3X SSC, 20% deionized formamide, 50°C. This allows simultaneous detection of at least two, and possibly all, of the mycobacterial species described in the current invention.

[0321] The following oligonucleotide probes were designed from the spacer region sequence of respectively *M. ulcerans*, *M. genavense*, *M. xenopi*, *M. simiae*, *M. fortuitum*, *M. malmoeense*, *M. celatum* and *M. haemophilum*:

MUL-ICG-1 : GGTTTCGGGATGTTGTCCCACC  
 5 MGV-ICG-1 : CGACTGAGGTCGACGTGGTGT  
 MGV-ICG-2 : GGTGTTTGAGCATTGAATAGTGGTTGC  
 MXE-ICG-1 : GTTGGGCAGCAGGCAGTAACC  
 10 MSI-ICG-1 : GCCGGCAACGGTTACGTGTTC  
 MFO-ICG-1 : TCGTTGGATGGCCTCGCACCT  
 15 MFO-ICG-2 : ACTTGGCGTGGGATGCGGGAA  
 MML-ICG-1: CGGATCGATTGAGTGCTTGTCCC  
 MML-ICG-2: TCTAAATGAACGCACTGCCGATGG  
 20 MCE-ICG-1: TGAGGGAGCCCGTGCCTGTA  
 MHP-ICG-1: CATGTTGGGCTTGATCGGGTGC

[0322] The probes were immobilized on a LiPA strip and hybridized with amplified biotinylated material derived from a set of representative mycobacterial species as described in example 2. Amplification of the spacer region was carried out by PCR using a primer set as described in example 2. The different strains used for specificity testing are shown in table 8 together with the hybridization results obtained. The strains were obtained from the collection of the Institute for Tropical Medicine, Antwerp, Belgium.

[0323] The probes tested (MSI-ICG1, MXE-ICG-1, MFO-ICG-1, MFO-ICG-2, MML-ICG-1, MML-ICG-2, MCE-ICG-1 and MHP-ICG-1) specifically detected *M. simiae*, *M. xenopi*, *M. fortuitum*, *M. malmoeense*, *M. celatum* and *M. haemophilum* respectively and showed no cross-hybridization with the other mycobacterial species tested. Thus, these probes allow a specific detection of mycobacterial species which were not further identifiable using the set of DNA probes described in example 2. *M. malmoeense* was classified in example 2 as a "MIC 4"-type, while the other species mentioned above were only hybridizing to the general probes MYC1/MYC22 for the genus *Mycobacterium*, and were thus classified in example 2 as "other mycobacterial species".

[0324] All tested *M. genavense* isolates reacted with MGV-ICG1 and MGV-ICG2, and not with MSI-ICG1 designed for *M. simiae*, closely related to *M. genavense*. A group of "intermediate" organisms, situated in between *M. simiae* and *M. genavense*, were received from the Tropical Institute of Medicine, Antwerp, where they were classified as "*M. simiae* - like" (strains 4358, 4824, 4833, 4844, 4849, 4857, 4859, 7375, 7379, 7730, 9745, 94-1228). These strains reacted only with probe MGV-ICG2 and not with probe MSI-ICG1 which specifically detects *M. simiae* strains *sensu stricto*. Sequencing of the 16S-23S rRNA spacer region of two of these "*M. simiae*-like" isolates (strains 7379 and 9745) (see SEQ ID NO 161 and 162) confirmed that they were more closely related to *M. genavense* than to *M. simiae*. A new probe MGV-ICG3 was designed to specifically detect this group of organisms, which possibly belong to a new species.

MGV-ICG 3 : TCGGGCCGCGTGTTCGTCAAA

[0325] This illustrates again that the use of DNA probes derived from the 16S-23S spacer region can be helpful in differentiating different groups of strains, which are also found indeterminate by classical taxonomic criteria. The use of these DNA probes may possibly lead to the description of new (sub)species within mycobacteria. In this case, the MGV-1 probe would react only with *M. genavense* strains *sensu stricto*, MGV-3 probe would react only with the intermediate "*M. simiae*-like" strains, and MGV-2 probe would detect both types of strains.

[0326] The probe MUL-ICG-1 reacted with all *M. ulcerans* strains tested, but also showed cross-hybridization with *M. marinum* strain ITG 7732. Sequencing of the spacer region of this *M. marinum* strain indeed revealed an identical sequence to that of *M. ulcerans* strain 1837 (see fig. 80). Further differentiation between *M. marinum* and *M. ulcerans* can be done using a probe from the 16S-rRNA gene of *M. ulcerans*, part of which is co-amplified with the spacer region when primers MYC P1 -P5 are used for amplification. A species-specific 16S rRNA probe for *M. ulcerans*, which can

work under the same hybridization conditions as the spacer probes for mycobacterium species differentiation, is for example :

TGGCCGGTGCAAAGGGCTG

(SEQ ID NO 216)

[0327] The above paragraph shows that, although it is preferable to use probes derived from the spacer region, it is also possible, and sometimes necessary, to combine the spacer probes with probes derived from other gene sequences, e.g. the 16S rRNA gene. Here again, these additional probes are selected such that they show the desired hybridization characteristics under the same hybridization and wash conditions as the spacer probes.

[0328] For M. kansasii, additional strains to the ones mentioned in example 2 have been tested with probes MKA-ICG-1, 2, 3 and 4 described in example 2. Since none of these probes was entirely satisfactory, additional probes were designed for M. kansasii detection. Therefore, the spacer region of some of the additional M. kansasii strains ITG 6328, 8698 and 8973 was sequenced (see fig.90 to 92). These strains were also obtained from the Institute of Tropical Medicine in Antwerp, Belgium. Apparently, M. kansasii strains constitute a quite heterogeneous group, with remarkable differences in the spacer sequence between different strains. Additional probes MKA-ICG-5, 6, 7, 8, 9 and 10 were designed, all hybridizing again under the same conditions as those earlier described, i.e. 3X SSC, 20% deionized formamide, 50°C. The probes were tested with a collection of test strains obtained from the Institute of Tropical Medicine, Antwerp, Belgium, and results are shown in table 8.

[0329] None of the M. kansasii probes hybridizes with a species other than M. kansasii, as far as tested. However, due to the heterogeneous character of this species, none of the M. kansasii probes hybridizes with all M. kansasii strains. The different M. kansasii probes recognize different strains of M. kansasii. This differential hybridization may be of clinical significance. On the other hand, if detection of all M. kansasii strains is desirable, a combination of different M. kansasii probes can be envisaged.

Table 8: additional mycobacterial probes

species/type	strain	MUL ICG-1	MGV ICG- 1 2 3	MXE ICG-1	MFO ICG-1 ICG-2	MSI ICG-1	MML ICG-1 ICG-2	MCE ICG-1	MHP ICG-1
M. tuberculosis	8004	-	-	-	-	-	-	-	-
M. avium	5887	-	-	-	-	-	-	-	-
M. intracellulare	5915 5913	-	-	-	-	-	-	-	-
MIC 3.1 strain	1812	-	-	-	-	-	-	-	-
MIC-4 strain	8724	-	-	-	-	-	-	-	-
M. scrofulaceum	4979	-	-	-	-	-	-	-	-
M. kansasii	4987 2795 6238 6362 8698 8973 8974 8971	- - - - - - - -	- - - - - - - -	- - - - - - - -	- - - - - - - -	- - - - - - - -	- - - - - - - -	- - - - - - - -	- - - - - - - -
M. ulcerans	1837 3129 5114 5115	+ + + +	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -
M. marinum	7732	+	-	-	-	-	-	-	-
M. malmoense	4832 4842	- -	- -	- -	- -	- -	+ +	- -	- -
M. goodii	7703	-	-	-	-	-	-	-	-

[illegible]

· = negative reaction, + = positive reaction, w = weak reaction, ± = variable reaction, blanc = non tested

Table 8 continued

species/type	strain	MKA ICG-3	MKA ICG-4	MKA ICG-5	MKA ICG-6	MKA ICG-7	MKA ICG-8	MKA ICG-9	MKA- ICG-10
M. tuberculosis	8004	-	-	-	-	-	-	-	-
M. avium	5887	-	-	-	-	-	-	-	-
M. intracellulare	5915 5913	-	-	-	-	-	-	-	-
MIC 3.1 strain	1812	-	-	-	-	-	-	-	-
MIC-4 strain	8724	-	-	-	-	-	-	-	-
M. scrofulaceum	4979	-	-	-	-	-	-	-	-
M. kansasii	4987 2795 6238 6362 8698 8973 8974 8971	+ + + + - - - -	+ + - - - - - -	- - + + - - - -	- - - - - + + +	- - - - + - - -	- - + + - + + +	- - + + + + + w - - -	+ + + + + + + +
M. ulcerans	1837 3129 5114 5115	-	-	-	-	-	-	-	-
M. marinum	7732	-	-	-	-	-	-	-	-
M. malmoense	4832 4842	-	-	-	-	-	-	-	-
M. goodii	7703	-	-	-	-	-	-	-	-



**Table 8 continued**

[illegible]

### EXAMPLE 8: Brucella

**[0330]** Brucellosis is a very widespread and economically important zoonosis which also affects humans.

[0331] For the identification of Brucella spp., mainly bacteriological and immunological detection techniques are

being used. These tests are time-consuming and often give false-positive results. Quick and reliable identification methods are being developed, mainly based on DNA amplification and hybridization.

[0332] Specific detection of *Brucella* spp. based on the amplification of a 43 kDa outer membrane protein (Fekete A. et al., 1990) or of a part of the 16S rRNA gene (Herman and De Ridder, 1992) were already described.

5 [0333] In order to develop specific DNA probes and primers for the detection of *Brucella* spp. we analyzed the 16S-23S rRNA gene spacer region. Using conserved primers (sequences are given in example 1) the spacer region was amplified and subsequently cloned into the Bluescript SK+ vector following the same procedures as in example 1. The obtained amplicon of about 1400 bp in length was cloned for the following *Brucella* species:

- 10 - *Brucella abortus* NIDO Tulya biovar 3 (SEQ ID NO 154)  
 - *Brucella melitensis* NIDO biovar 1 (SEQ ID NO 131)  
 - *Brucella suis* NIDO biovar 1 (SEQ ID NO 132)

15 *Hind*III digestion of the constructs, followed by subcloning of the obtained fragments (n=3) facilitated the sequencing of the spacer region for the three described *Brucella* spp..

Fig. 56, 57 and 79 represent the sequences of the spacer regions obtained for the above-mentioned strains of respectively *Brucella melitensis*, *Brucella suis* and *Brucella abortus*.

Due to the high homology of these spacer region sequences between different *Brucella* species, no species-specific DNA probes were deduced from this sequence information, and only genus-specific probes were designed.

20 [0334] For this purpose, the following probes were chemically synthesized:

BRU-ICG 1 : CGTGCCGCCTTCGTTTCTCTTT

25

BRU-ICG 2 : TTCGCTTCGGGGTGGATCTGTG

BRU-ICG 3 : GCGTAGTAGCGTTTGCGTCGG

BRU-ICG 4 : CGCAAGAAGCTTGCTCAAGCC

30 The oligonucleotides were immobilized on a membrane strip and following reverse hybridization with biotinylated PCR fragments, the hybrids were visualized using a precipitation reaction. The hybridization results of the immobilized probes with different *Brucella* spp. and related organisms are represented in the table 9.

35 [0335] These hybridization results show that probes BRU-ICG 2, BRU-ICG 3 and BRU-ICG 4 are specific for *Brucella* spp. and can be used in a reverse hybridization assay for detection of these pathogens. Probe BRU-ICG 1 cross-hybridizes with *Ochrobactrum anthropi* and *Rhizobium loti* strains, which are two taxonomically highly related organisms, but which are not expected to be present in the same sample material as used for *Brucella* detection.

[0336] As described in previous examples (e.g. 3 and 4) also for *Brucella* specific primers were chosen from the 16S-23S rRNA spacer region, in order to specifically amplify the spacer region from *Brucella* strains.

40 [0337] BRU-P1 and BRU-P2 are used as upper primers, while BRU-P3 and BRU-P4 are used as lower primers. When used in a nested PCR assay the combination BRU-P1/BRU-4 is the outer primerset whereas the combination BRU-P2/BRU-P3 is the inner primerset.

45	BRU-P1 : TCGAGAATTGGAAAGAGGTC	204
	BRU-P2 : AAGAGGTCGGATTTATCCG	205
	BRU-P3 : TTCGACTGCAAATGCTCG	206
50	BRU-P4 : TCTTAAAGCCGCATTATGC	207

TABLE 9

55

TAXA TESTED	n	BRU-ICG 1	BRU-ICG 2	BRU-ICG 3	BRU-ICG 4
<i>Brucella abortus</i>	6	+	+	+	+
<i>Brucella suis</i>	3	+	+	+	+

TABLE 9 (continued)

	TAXA TESTED	n	BRU-ICG 1	BRU-ICG 2	BRU-ICG 3	BRU-ICG 4
	<u>Brucella melitensis</u>	4	+	+	+	+
5	<u>Brucella ovis</u>	2	+	+	+	+
	<u>Brucella canis</u>	2	+	+	+	+
	<u>Brucella neotomae</u>	1	+	+	+	+
	<u>Phyllobacterium rubiacearum</u>	1	-	-	NT	NT
	<u>Ochrobactrum anthropi</u>	8	+	-	-	-
10	<u>Agrobacterium tumefaciens</u>	2	-	-	NT	NT
	<u>Agrobacterium rhizogenes</u>	1	-	-	NT	NT
	<u>Mycoplana dimorpha</u>	1	-	-	NT	NT
	<u>Rhizobium loti</u>	1	+	-	-	-
15	<u>Rhizobium meliloti</u>	1	-	-	NT	NT
	<u>Rhizobium leguminosarum</u>	1	-	-	NT	NT
	<u>Bradyrhizobium japonicum</u>	1	-	-	NT	NT
	<u>Brochothrix thermosphacta</u>	1	-	-	NT	NT
	<u>Brochothrix campestris</u>	1	-	-	NT	NT
20	<u>Bacillus cereus</u>	3	-	-	NT	NT
	<u>Bacillus brevis</u>	2	-	-	NT	NT
	<u>Bacillus coagulans</u>	1	-	-	NT	NT
	<u>Bacillus pumilis</u>	1	-	-	NT	NT
25	<u>Bacillus macerans</u>	1	-	-	NT	NT
	<u>Bacillus lentus</u>	1	-	-	NT	NT
	<u>Bacillus firmus</u>	2	-	-	NT	NT
	<u>Bacillus subtilis</u>	2	-	-	NT	NT
	<u>Bacillus megaterium</u>	1	-	-	NT	NT
30	<u>Enterococcus faecalis</u>	1	-	-	NT	NT
	<u>Enterococcus faecium</u>	1	-	-	NT	NT
	<u>Enterococcus durans</u>	1	-	-	NT	NT
	<u>Lactobacillus lactis</u>	3	-	-	NT	NT
35	<u>Lactobacillus casei</u>	1	-	-	NT	NT
	<u>Leuconostoc lactis</u>	1	-	-	NT	NT
	<u>Escherichia coli</u>	1	-	-	NT	NT
	<u>Hafnia halvei</u>	1	-	-	NT	NT
	<u>Clostridium tyrobutyricum</u>	1	-	-	NT	NT
40	<u>Clostridium perfringens</u>	1	-	-	NT	NT
	<u>Clostridium sporogenes</u>	1	-	-	NT	NT
	<u>Clostridium acetobutyricum</u>	1	-	-	NT	NT
	<u>Staphylococcus aureus</u>	1	-	-	NT	NT
45	<u>Salmonella enteritidis</u>	1	-	-	NT	NT
	<u>Yersinia enterocolitica</u>	1	-	-	NT	NT
	<u>Listeria monocytogenes</u>	1	-	-	NT	NT
	<u>Listeria ivanovii</u>	1	-	-	NT	NT
	<u>Listeria seeligeri</u>	1	-	-	NT	NT
50	<u>Listeria welshimeri</u>	1	-	-	NT	NT
	<u>Listeria innocua</u>	1	-	-	NT	NT
	<u>Listeria murrayi</u>	1	-	-	NT	NT
	<u>Listeria grayi</u>	1	-	-	NT	NT
55	NT = Not tested      n = number of strains tested					

**EXAMPLE 9: *Staphylococcus aureus***

5 [0338] *Staphylococcus aureus* is the staphylococcal species most commonly associated with human and animal infections. *Staphylococcus aureus* strains have been identified as important etiologic agents in both community-acquired and nosocomial infections. Recently nosocomial infection with methicillin-resistant *S. aureus* (MRSA) appear to be increasingly prevalent in many countries. The strains belonging to this species are also causative agents of food spoilage and poisoning.

10 [0339] In order to discriminate in a fast and specific way *S. aureus* strains from other staphylococci, the use of molecular techniques based on DNA probes and/or PCR were already described in the literature. Examples of target genes used for the development of these DNA based assays are the 16S rRNA gene (De Buyser et al., 1992; Geha et al, 1994), the *mecA* gene (Ubukata et al., 1992; Shimaoka et al., 1994 ) and the *nuc* gene (Brakstad et al., 1992; Chesneau et al., 1993).

15 [0340] As a target for the development of specific DNA probes we chose the 16S-23S rRNA gene spacer region. Amplification using conserved primers derived from the 16S and the 23S rRNA genes (sequences, see example 1) showed that the pattern obtained was not similar in all *S. aureus* strains tested. A lot of variation was seen in either the number of fragments obtained and in the size of these different fragments.

20 [0341] One spacer region from strain UZG 5728 and four spacer regions (differing in length) from strain UZG 6289 were cloned into Bluescript SK+ vector and subsequently sequenced. The sequences are represented in fig. 64 to fig. 68 (SEQ ID NO 139 to SEQ ID NO 143). For the development of specific DNA probes these different spacer regions were compared to each other and to the spacer region derived from *Staphylococcus epidermidis* strain UZG CNS41 (SEQ ID NO 144).

[0342] The following probes were chemically synthesized :

25 STAU-ICG 1 : TACCAAGCAAACCGAGTGAATAAAGAGTT

STAU-ICG 2 : CAGAAGATGCGGAATAACGTGAC

STAU-ICG 3 : AACGAAGCCGTATGTGAGCATTTGAC

30 STAU-ICG 4 : GAACGTAACCTTCATGTTAACGTTTGACTTAT

[0343] The oligonucleotides were immobilized on a membrane strip and following reverse hybridization with biotinylated PCR fragments, the hybrids were visualized using a colorimetric precipitation reaction.

35 [0344] The hybridization results of the immobilized probes with different *Staphylococcus* spp. and non-staphylococcal organisms are represented in Table 10.

[0345] These hybridization results show that only probes STAU-ICG 3 and STAU-ICG 4 are specific for *Staphylococcus aureus* strains. Probe STAU-ICG 1 reacts with all *Staphylococcus* spp. tested and probe STAU-ICG 2 cross-hybridizes with the *S. lugdinensis* strain.

40 Neither probe STAU-ICG 3 nor probe STAU-ICG 4 detects all *S. aureus* strains tested, but when both probes are used simultaneously in a LiPA assay, all *S. aureus* strains tested hybridize with one of these probes or with both.

45

50

55

Table 10

Strains tested	n	STAU-ICG 1	STAU-ICG 2	STAU-ICG 3	STAU-ICG 4
<i>Staphylococcus aureus</i>	13	+	+	+	+
<i>Staphylococcus aureus</i>	10	+	+	-	+
<i>Staphylococcus aureus</i>	3	+	+	w	+
<i>staphylococcus aureus</i>	1	+	+	+	-
<i>Staphylococcus epidermidis</i>	11	+	-	-	-
<i>Staphylococcus saprophyticus</i>	1	+	-	-	-
<i>Staphylococcus haemolyticus</i>	1	+	-	-	-
<i>Staphylococcus capitis</i>	1	+	+	-	-
<i>Staphylococcus lugdinensis</i>	1	+	-	-	-
<i>Staphylococcus hominis</i>	1	+	-	-	-
<i>Bordetella pertussis</i>	1	+	-	-	-
<i>Bordetella parapertussis</i>	1	-	-	-	-
<i>Bordetella bronchiseptica</i>	1	-	-	-	-
<i>Mycobacterium tuberculosis</i>	1	-	-	-	-
<i>Mycobacterium avium</i>	1	-	-	-	-
<i>Moraxella catarrhalis</i>	4	-	-	-	-
<i>Haemophilus influenzae</i>	2	-	-	-	-
<i>Streptococcus pneumoniae</i>	3	-	-	-	-
<i>Pseudomonas cepacia</i>	1	-	-	-	-
<i>Pseudomonas aeruginosa</i>	3	-	-	-	-
<i>Acinetobacter calcoaceticus</i>	1	-	-	-	-

## REFERENCES

[0346] Asseline U, Delarue M, Lancelot G, Toulme F, Thuong N (1984) Nucleic acid-binding molecules with high affinity and base sequence specificity: intercalating agents covalently linked to oligodeoxynucleotides. Proc. Natl. Acad. Sci. USA 81(11):3297-301.

- [0347] Barany F (1991). Genetic disease detection and DNA amplification using cloned thermostable ligase. *Proc Natl Acad Sci USA* 88: 189-193.
- [0348] Bej A, Mahbubani M, Miller R, Di Cesare J, Haff L, Atlas R (1990) Multiplex PCR amplification and immobilized capture probes for detection of bacterial pathogens and indicators in water. *Mol Cell Probes* 4:353-365.
- 5 [0349] Boddingtonhaus B, Rogall T, Flohr T, Blocker H, Bottger E (1990). Detection and identification of *Mycobacteria* by amplification of rRNA. *Journal of Clinical Microbiology*, 28 : 1751-1759.
- [0350] Brakstad, O.G., K. Aasbakk, and J.A. Maeland. 1992. Detection of *Staphylococcus aureus* by polymerase chain reaction amplification of the *nuc* gene. *J. Clin. Microbiol.* 30:1654-1660.
- [0351] Bubert A, Kohler S, Goebel W (1992). The homologous and heterologous regions within the *iap* gene allow genus- and species-specific identification of *Listeria* spp. by polymerase chain reaction. *Applied and Environmental Microbiology*, 58 : 2625-2632.
- 10 [0352] Buck G, O'Hara L, Summersgill J (1992). Rapid, sensitive detection of *Mycoplasma pneumoniae* in simulated clinical specimens by DNA amplification. *Journal of Clinical Microbiology*, 30 : 3280-3283.
- [0353] Bukh J, Purcell R, Miller R (1993). At least 12 genotypes ... *PNAS* 90,8234-8238.
- 15 [0354] Chesneau, O., J. Allignet and N. El Solh. 1993. Thermonuclease gene as a target nucleotide sequence for specific recognition of *Staphylococcus aureus*. *Mol. Cell. Probes*. 7:301-310.
- [0355] Chomczynski P, Sacchi N (1987) Single step method of RNA isolation by acid guanidinium thiocyanate-phenol-chloroform extraction. *Anal Biochem* 162:156-159.
- [0356] Compton J (1991). Nucleic acid sequence-based amplification. *Nature*, 350: 91-92.
- 20 [0357] Datta A, Moore M, Wentz B, Lane J (1993). Identification and enumeration of *Listeria monocytogenes* by nonradioactive DNA probe colony hybridization. *Applied and Environmental Microbiology*, 59 : 144-149.
- [0358] De Buyser, M., A. Morvan, S. Aubert, F. Dilasser and N. El Solh. 1992. Evaluation of a ribosomal RNA gene probe for the identification of species and subspecies within the genus *Staphylococcus*. *J. Gen. Microbiol.* 138:889-899.
- [0359] Duck P (1990). Probe amplifier system based on chimeric cycling oligonucleotides. *Biotechniques* 9, 142-147.
- 25 [0360] Farber J, Peterkin P (1991). *Listeria monocytogenes*, a food-borne pathogen. *Microbiological Reviews*, 55: 476-511.
- [0361] Fekete, A., J.A. Bantle, S.M. Balling and M.R. Sanborn. 1990. Preliminary development of a diagnostic test for *Brucella* using polymerase chain reaction. *J. Appl. Bacteriol.* 69:216-227.
- [0362] Frothingham R, Wilson K (1993). Sequence-based differentiation of strains in the *Mycobacterium avium* complex. *Journal of Bacteriology*, 175.
- 30 [0363] Frothingham R, Wilson K (1994). Molecular phylogeny of the *Mycobacterium avium* complex demonstrates clinically meaningful divisions. *J Infect Diseases*, 169: 305-312.
- [0364] Geha, D.J., J.R. Uhl, C.A. Gustaferrero, and D.H. Persing. 1994. Multiplex PCR for identification of methicillin-resistant staphylococci in the clinical laboratory. *J. Clin. Microbiol.* 32:1768-1772.
- 35 [0365] Golsteyn Thomas E, King R, Burchak J, Gannon V (1991). Sensitive and specific detection of *Listeria monocytogenes* in milk and ground beef with the polymerase chain reaction. *Applied and Environmental Microbiology*, 57 : 2576-2580.
- [0366] Guatelli J, Whitfield K, Kwok D, Barringer K, Richman D, Gengeras T (1990) Isothermal, in vitro amplification of nucleic acids by a multienzyme reaction modeled after retroviral replication. *Proc Natl Acad Sci USA* 87: 1874-1878.
- 40 [0367] Herman L, De Ridder H (1993). Evaluation of a DNA-probe assay for the identification of *Listeria monocytogenes*. *Milchwissenschaft*, 48 : 126-128.
- [0368] Herman, L. and H. De Ridder. 1992. Identification of *Brucella* spp. by using the polymerase chain reaction. *Appl. Env. Microbiol.* 58:2099-2101.
- [0369] Jacobs K, Rudersdorf R, Neill S, Dougherty J, Brown E, Fritsch E (1988) The thermal stability of oligonucleotide duplexes is sequence independent in tetraalkylammonium salt solutions: application to identifying recombinant DNA clones. *Nucl Acids Res* 16:4637-4650.
- 45 [0370] Jatón K, Sahlí R, Bille J (1992). Development of polymerase chain reaction assays for detection of *Listeria monocytogenes* in clinical cerebrospinal fluid samples. *Journal of Clinical Microbiology*, 30 : 1931-1936.
- [0371] Jonas V, Aldan M, Curry J, Kamisango K, Knott C, Lankford R, Wolfe J, Moore D (1993). Detection and identification of *Mycobacterium tuberculosis* directly from sputum sediments by amplification of rRNA. *Journal of Clinical Microbiology*, 31: 2410-2416.
- 50 [0372] Kempell K et al. (1992). The nucleotide sequence of the promoter, 16S rRNA and spacer region of the ribosomal RNA operon of *Mycobacterium tuberculosis* and comparison with *M. leprae* precursor rRNA. *Journal of Gen Microbiol*, 138: 1717-1727.
- 55 [0373] Kwok D, Davis G, Whitfield K, Chappelle H, Dimichele L, Gengeras T (1989). Transcription-based amplification system and detection of amplified human immunodeficiency virus type 1 with a bead-based sandwich hybridization format. *Proc Natl Acad Sci USA*, 86: 1173-1177.
- [0374] Kwok S, Kellogg D, McKinney N, Spasic D, Goda L, Levenson C, Sinisky J, (1990). Effects of primer-template

mismatches on the polymerase chain reaction: Human immunodeficiency virus type 1 model studies. Nucl. Acids Res., 18: 999.

[0375] Landgren U, Kaiser R, Sanders J, Hood L (1988). A ligase-mediated gene detection technique. Science 241: 1077-1080.

5 [0376] Lizardi P, Guerra C, Lomeli H, Tussie-Luna I, Kramer F (1988) Exponential amplification of recombinant RNA hybridization probes. Bio/Technology 6:1197-1202.

[0377] Loeffelholz M, Lewinski C, Silver S, Purohit A, Herman S, Buonagurio D, Dragon E (1992). Detection of *Chlamydia trachomatis* in endocervical specimens by polymerase chain reaction. Journal of Clinical Microbiology, 30: 2847-2851.

10 [0378] Lomeli H, Tyagi S, Printchard C, Lizardi P, Kramer F (1989) Quantitative assays based on the use of replicatable hybridization probes. Clin Chem 35: 1826-1831.

[0379] Maniatis T, Fritsch E, Sambrook J (1982) Molecular cloning: a laboratory manual. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY.

15 [0380] Matsukura M, Shinozuka K, Zon G, Mitsuya H, Reitz M, Cohen J, Broder S (1987) Phosphorothioate analogs of oligodeoxynucleotides : inhibitors of replication and cytopathic effects of human immunodeficiency virus. Proc. Natl. Acad. Sci. USA 84(21):7706-10.

[0381] McIntosh I, Govan J, Brock D (1992). Detection of *Pseudomonas aeruginosa* in sputum from cystic fibrosis patients by the polymerase chain reaction. Molecular and Cellular Probes, 6: 299-304.

20 [0382] Miller P, Yano J, Yano E, Carroll C, Jayaram K, Ts'o P (1979) Nonionic nucleic acid analogues. Synthesis and characterization of dideoxyribonucleoside methylphosphonates. Biochemistry 18(23):5134-43.

[0383] Nielsen P, Egholm M, Berg R, Buchardt O (1991) Sequence-selective recognition of DNA by strand displacement with a thymine-substituted polyamide. Science 254(5037):1497-500.

[0384] Nielsen P, Egholm M, Berg R, Buchardt O (1993) Sequence specific inhibition of DNA restriction enzyme cleavage by PNA. Nucleic-Acids-Res. 21(2):197-200.

25 [0385] Ninet B, Bannerman E, Bille J (1992). Assessment of the accuprobe *Listeria monocytogenes* culture identification reagent kit for rapid colony confirmation and its application in various enrichment broths. Applied and Environmental Microbiology, 58 : 4055-4059.

[0386] Ogle J, Janda J, Woods D, Vasil M (1987). Characterization and use of a DNA probe as an epidemiological marker for *Pseudomonas aeruginosa*. The Journal of Infectious Diseases, 155: 119.

30 [0387] Ossewaarde J, Rieffe M, Rozenberg-Arska M, Ossenkoppele P, Nawrocki R, Van Loon A (1992). Development and clinical evaluation of a polymerase chain reaction test for detection of *Chlamydia trachomatis*. Journal of Clinical Microbiology, 30: 2122-2128.

[0388] Rogall T, Wolters J, Flohr T, Bottger E (1990). Towards a phylogeny and definition of species at the molecular level within the genus *Mycobacterium*. Int. J. Syst. Bacteriol. 40 : 323-330.

35 [0389] Rossau R, Michielsen A, Jannes G, Duhamel M, Kersten K, Van Heuverswyn H. DNA probes for *Bordetella* species and a colorimetric reverse hybridization assay for the detection of *Bordetella pertussis*. Mol. Cell. Probes 6 : 281-289, 1992

[0390] Saiki R, Gelfand D, Stoffel S, Scharf S, Higuchi R, Horn G, Mullis K, Erlich H (1988). Primer-directed enzymatic amplification of DNA with a thermostable DNA polymerase. Science 239: 487-491.

40 [0391] Saiki R, Walsh P, Levenson C, Erlich H (1989) Genetic analysis of amplified DNA with immobilized sequence-specific oligonucleotide probes (1989) Proc Natl Acad Sci USA 86:6230-6234.

[0392] Saito H, Tomioka H, Sato K, Hiromichi T, Tsukamura M, Kuze F, Asano K (1989). Identification and partial characterization of *Mycobacterium avium* and *Mycobacterium intracellulare* by using DNA probes. Journal of Clinical Microbiology, 27 : 994-997.

45 [0393] Samadpour M, Moseley S, Lory S (1988). Biotinylated DNA probes for exotoxin A and pilin genes in the differentiation of *Pseudomonas aeruginosa* strains. Journal of Clinical Microbiology, 26 : 2319-2323.

[0394] Sano T, Smith C, Cantor C (1992) Immuno-PCR: very sensitive antigen detection by means of specific antibody-DNA conjugates. Science 258:120-122.

50 [0395] Shimaoka, M., M. Yoh, A. Segawa, Y. Takarada, K. Yamamoto and T. Honda. 1994. Development of enzyme-labeled oligonucleotide probe for detection of *mecA* gene in methicillin-resistant *Staphylococcus aureus*. J. Clin. Microbiol. 32:1866-1869.

[0396] Stuyver L, Rossau R, Wyseur A, Duhamel M, Vanderborcht B, Van Heuverswyn H, Maertens G (1993) Typing of hepatitis C virus (HCV) isolates and characterization of new (sub)types using a Line Probe Assay. J Gen Virology, 74: 1093-1102.

55 [0397] Suzuki Y et al. (1988). Complete nucleotide sequence of the 16S rRNA gene of *Mycobacterium bovis* BCG. J Bacteriol, 170: 2886-2889.

[0398] Taylor-Robinson D, Gilroy C, Thomas B, Keat A (1992). Detection of *Chlamydia trachomatis* DNA in joints of reactive arthritis patients by polymerase chain reaction. Lancet 340 : 81-82.

- [0399] Telenti A, Marchesi F, Balz M, Bally F, Bottger E, Bodmer T (1993). Rapid identification of *Mycobacteria* to the species level by polymerase chain reaction and restriction enzyme analysis. *Journal of Clinical Microbiology*, 31: 175-178.
- [0400] Tomioka H, Saito H, Sato K, Tasaka H, Dawson J (1993). Identification of *Mycobacterium avium* complex strains belonging to serovars 21-28 by three commercial DNA probe tests. *Tubercle and Lung Disease*, 74 : 91-95.
- [0401] Ubukata, K., S. Nakagami, A. Nitta, A. Yamane, S. Kawakami, M. Suguria and M. Konno. 1992. Rapid detection of the *mecA* gene in methicillin-resistant staphylococci by enzymatic detection of polymerase chain reaction products. *J. Clin. Microbiol.* 30:1728-1733.
- [0402] Van der Giessen, J et al (1994). Comparison of the 23S rRNA genes and the spacer region between the 16S and 23S rRNA genes of the closely related *M. avium* and *M. paratuberculosis* and the fast-growing *M. phlei*. *Microbiology*, 140: 1103-1108.
- [0403] Vanechoutte M, De Beenhouwer H, Claeys G, Verschraegen G, De Rouck A, Paepe N, Elaichouni A, Portaels F (1993). Identification of *Mycobacterium* species by using amplified ribosomal DNA restriction analysis. *Journal of Clinical Microbiology*, 31: 2061-2065.
- [0404] Van Kuppeveld F, Van Der Logt J, Angulo A, Van Zoest M, Quint W, Niesters H, Galama J, Melchers W (1992). Genus- and species-specific identification of mycoplasmas by 16S rRNA amplification. *Applied and Environmental Microbiology*, 58 : 2606-2615.
- [0405] Walker G, Little M, Nadeau J, Shank D (1992). Isothermal in vitro amplification of DNA by a restriction enzyme/DNA polymerase system. *Proc Natl Acad Sci USA* 89:392-396.
- [0406] Woods G, Young A, Scott J, Blair T, Johnson A (1990). Evaluation of a nonisotopic probe for detection of *Chlamydia trachomatis* in endocervical specimens. *Journal of Clinical Microbiology*, 28 : 370-372.
- [0407] Wu D, Wallace B (1989). The ligation amplification reaction (LAR) - amplification of specific DNA sequences using sequential rounds of template-dependent ligation. *Genomics* 4:560-569.



## SEQUENCE LISTING

## (1) GENERAL INFORMATION:

## (i) APPLICANT:

- (A) NAME: Innogenetics N.V.
- (B) STREET: Industriepark Zwijnaarde 7 Bus 4
- (C) CITY: Gent
- (E) COUNTRY: Belgium
- (F) POSTAL CODE (ZIP): 9052
- (G) TELEPHONE: 00-32-09.241.07.11
- (H) TELEFAX: 00-32-09.241.07.66

(ii) TITLE OF INVENTION: SIMULTANEOUS DETECTION, IDENTIFICATION AND DIFFERENTIATION OF EUBACTERIAL TAXA USING A HYBRIDIZATION ASSAY

(iii) NUMBER OF SEQUENCES: 216

## (iv) COMPUTER READABLE FORM:

- (A) MEDIUM TYPE: Floppy disk
- (B) COMPUTER: IBM PC compatible
- (C) OPERATING SYSTEM: PC-DOS/MS-DOS
- (D) SOFTWARE: PatentIn Release #1.0, Version #1.25 (EPO)

## (2) INFORMATION FOR SEQ ID NO: 1:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 25 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

ACTGGATAGT GGTTCGAGC ATCTA

25

## (2) INFORMATION FOR SEQ ID NO: 2:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

CTTCTGAATA GTGGTTGCGA GCATCT

26

5

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 25 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

10

(ii) MOLECULE TYPE: cDNA

15

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

GGGTGCATGA CAACAAAGTT GGCCA

25

20

(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 24 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

25

(ii) MOLECULE TYPE: cDNA

30

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

GACTTGTTCC AGGTGTTGTC CCAC

24

40

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 21 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

45

(ii) MOLECULE TYPE: cDNA

50

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

CGGCTAGCGG TGGCGTGTTT C

21

5 (2) INFORMATION FOR SEQ ID NO: 6:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 26 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
10 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

15 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

20

CAACAGCAAA TGATTGCCAG ACACAC

26

(2) INFORMATION FOR SEQ ID NO: 7:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
25 (D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

GAGGGGTTCC CGTCTGTAGT G

21

40

(2) INFORMATION FOR SEQ ID NO: 8:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
45 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

50

(iii) ANTI-SENSE: NO

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

TGAGGGGTTC TCGTCTGTAG TG

22

## (2) INFORMATION FOR SEQ ID NO: 9:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

CACTCGGTTCG ATCCGTGTGG A

21

## (2) INFORMATION FOR SEQ ID NO: 10:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

TCGGTCCGTC CGTGTGGAGT C

21

## (2) INFORMATION FOR SEQ ID NO: 11:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

GTGGCCGGCG TTCATCGAAA

20

## (2) INFORMATION FOR SEQ ID NO: 12:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 25 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

GCATAGTCCT TAGGGCTGAT GCGTT

## (2) INFORMATION FOR SEQ ID NO: 13:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 25 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

GCTGATGCGT TCGTCGAAAT GTGTA

## (2) INFORMATION FOR SEQ ID NO: 14:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 23 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

CTGATGCGTT CGTCGAAATG TGT

(2) INFORMATION FOR SEQ ID NO: 15:

5 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 22 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15:

TGATGCGTTC GTCGAAATGT GT

22

20

(2) INFORMATION FOR SEQ ID NO: 16:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 27 base pairs  
 (B) TYPE: nucleic acid  
 25 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

30

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:

GGCTGATGCG TTCGTCGAAA TGTGTAA

27

(2) INFORMATION FOR SEQ ID NO: 17:

40 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 24 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

45

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17:

ACTAGATGAA CGCGTAGTCC TTGT

24

55

(2) INFORMATION FOR SEQ ID NO: 18:

5 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 22 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

10 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18:

TGGACGAAAA CCGGGTGCAC AA

22

20 (2) INFORMATION FOR SEQ ID NO: 19:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 38 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 25 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

30 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19:

35 GTGTAATTTT TTTTAACT CTTGTGTGTA AGTAAGTG

38

(2) INFORMATION FOR SEQ ID NO: 20:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 21 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 40 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

45 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

TGGCCGGCGT GTTCATCGAA A

21

55 (2) INFORMATION FOR SEQ ID NO: 21:

5 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 26 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

10 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:  
 GCACTTCAAT TGGTGAAGTG CGAGCC 26

(2) INFORMATION FOR SEQ ID NO: 22:

20 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 19 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:  
 GCGTGGTCTT CATGGCCGG 19

35 (2) INFORMATION FOR SEQ ID NO: 23:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 18 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: cDNA

45 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 23:  
 ACGCGTGGTC CTTCTGG 18

(2) INFORMATION FOR SEQ ID NO: 24:

55 (i) SEQUENCE CHARACTERISTICS:



(A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

5

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

10

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 24:

15

TCGGCTCGTT CTGAGTGGTG TC

22

(2) INFORMATION FOR SEQ ID NO: 25:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 23 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

20

(ii) MOLECULE TYPE: cDNA

25

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25:

GATGCGTTTG CTACGGGTAG CGT

23

35

(2) INFORMATION FOR SEQ ID NO: 26:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 23 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

40

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

45

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26:

50

GATGCGTTGC CTACGGGTAG CGT

23

(2) INFORMATION FOR SEQ ID NO: 27:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 23 base pairs

55

(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

5

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

ATGCGTTGCC CTACGGGTAG CGT

15

23

(2) INFORMATION FOR SEQ ID NO: 28:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

20

(ii) MOLECULE TYPE: cDNA

25

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

CGGGCTCTGT TCGAGAGTTG TC

22

(2) INFORMATION FOR SEQ ID NO: 29:

35

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 25 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

40

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

45

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

50

GGTGTGGACT TTGACTTCTG AATAG

25

(2) INFORMATION FOR SEQ ID NO: 30:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid

55

(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

CGGCAAAACG TCGGACTGTC A

21

15

(2) INFORMATION FOR SEQ ID NO: 31:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

20

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

25

(iii) ANTI-SENSE: NO

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:

AACACCCTCG GGTGCTGTCC

20

(2) INFORMATION FOR SEQ ID NO: 32:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

35

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

40

(iii) ANTI-SENSE: NO

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

GTATGCGTTG TCGTTCGCGG C

21

50

(2) INFORMATION FOR SEQ ID NO: 33:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single

55

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

5 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:

CGTGAGGGGT CATCGTCTGT AG

22

15 (2) INFORMATION FOR SEQ ID NO: 34:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 21 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 20 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

25 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34:

30 TGGTGTGCTG CGTGATCCGA T

21

(2) INFORMATION FOR SEQ ID NO: 35:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 26 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 35 (D) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 35:

TGAATGTTCG TGGATGAACA TTGATT

26

50 (2) INFORMATION FOR SEQ ID NO: 36:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 23 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 55 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

CACTGGTGAT CATTCAAGTC AAG

23

(2) INFORMATION FOR SEQ ID NO: 37:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37:

TGAATGTTTCG TVVATGAACA TTGATTTCTG GTC

33

(2) INFORMATION FOR SEQ ID NO: 38:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 29 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:

CTCTTTTCACT GGTGATCATT CAAGTCAAG

29

(2) INFORMATION FOR SEQ ID NO: 39:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:

CAAGTAACCG AGAATCATCT GAAAGTGAAT C

(2) INFORMATION FOR SEQ ID NO: 40:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 36 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 40:

AAACAACCTT TACTTCGTAG AAGTAAATTG GTTAAG

(2) INFORMATION FOR SEQ ID NO: 41:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 32 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:

TGAGAGGTTA GTACTTCTCA GTATGTTTGT TC

(2) INFORMATION FOR SEQ ID NO: 42:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

5 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:

10 AGGCACTATG CTTGAAGCAT CGC

23

(2) INFORMATION FOR SEQ ID NO: 43:

(i) SEQUENCE CHARACTERISTICS:

15 (A) LENGTH: 38 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

20

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 43:

GTTCAGATAA ATAGGTAAC TTTATGACA CAAGTAAC

38

30 (2) INFORMATION FOR SEQ ID NO: 44:

(i) SEQUENCE CHARACTERISTICS:

35 (A) LENGTH: 36 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

40

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 44:

45

AGTTAGCATA AGTAGTGTA CTATTTATGA CACAAG

36

(2) INFORMATION FOR SEQ ID NO: 45:

(i) SEQUENCE CHARACTERISTICS:

50 (A) LENGTH: 26 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

55

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 45:

GGAAGAAGCC TGAGAAGGTT TCTGAC

26

10

(2) INFORMATION FOR SEQ ID NO: 46:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

15

(ii) MOLECULE TYPE: cDNA

20

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 46:

GCATTATAT GTAAGAGCAA GCATTCTATT TCA

33

(2) INFORMATION FOR SEQ ID NO: 47:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 22 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

30

35

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

40

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:

45

GAGTAGCGTG GTGAGGACGA GA

22

(2) INFORMATION FOR SEQ ID NO: 48:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: cDNA

55

(iii) HYPOTHETICAL: NO



(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 48:

GGATAACTGT CTTAGGACGG TTTGAC

26

10

(2) INFORMATION FOR SEQ ID NO: 49:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 30 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

15

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

20

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 49:

25

ATCGGTGGTA AATTAAACCC AAATCCCTGT

30

(2) INFORMATION FOR SEQ ID NO: 50:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 30 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

35

(iii) ANTI-SENSE: NO

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 50:

CAGTTCTGAA AGAACATTTT CGCTTCTTTC

30

45

(2) INFORMATION FOR SEQ ID NO: 51:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 30 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

55

(iii) ANTI-SENSE: NO

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 51:

CACCCATTAA TTTTTCGGT GTTAAAACCC

30

(2) INFORMATION FOR SEQ ID NO: 52:

10

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 31 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

15

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

20

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52:

25

CAAAACTGAA AACGACAATC TTTCTAGTTC C

31

(2) INFORMATION FOR SEQ ID NO: 53:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 30 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: cDNA

35

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53:

TACCAAGCAA AACCGAGTGA ATAAAGAGTT

30

45 (2) INFORMATION FOR SEQ ID NO: 54:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 23 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

55

(iii) ANTI-SENSE: NO

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 54:

CAGAAGATGC GGAATAACGT GAC

23

(2) INFORMATION FOR SEQ ID NO: 55:

10 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 26 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 55:

25 AACGAAGCCG TATGTGAGCA TTGAC

26

(2) INFORMATION FOR SEQ ID NO: 56:

30 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 31 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

35 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 56:

GAACGTAAC TCAATGTTAAC GTTGACTTA T

31

(2) INFORMATION FOR SEQ ID NO: 57:

45 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 27 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

55 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 57:

5

GCTTAAGTGC ACAGTGCTCT AACTGA

27

(2) INFORMATION FOR SEQ ID NO: 58:

(i) SEQUENCE CHARACTERISTICS:

10

- (A) LENGTH: 27 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

15

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 58:

CACGGTAATT AGTGTGATCT GACGAAG

27

(2) INFORMATION FOR SEQ ID NO: 59:

(i) SEQUENCE CHARACTERISTICS:

25

- (A) LENGTH: 22 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

35

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 59:

40

CGTGCCGCCT TCGTTTCTCT TT

22

(2) INFORMATION FOR SEQ ID NO: 60:

(i) SEQUENCE CHARACTERISTICS:

45

- (A) LENGTH: 22 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 60:

5 TTCGCTTCGG GGTGGATCTG TG 22

(2) INFORMATION FOR SEQ ID NO: 61:

(i) SEQUENCE CHARACTERISTICS:

- 10 (A) LENGTH: 28 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

15 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 61:

CAAACTGAC TTACGAGTCA CGTTTGAG 28

(2) INFORMATION FOR SEQ ID NO: 62:

25 (i) SEQUENCE CHARACTERISTICS:

- 30 (A) LENGTH: 25 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

35 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 62:

40 GATGTATGCT TCGTTATTCC ACGCC 25

(2) INFORMATION FOR SEQ ID NO: 63:

45 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

50 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 63:

GGTCAAACCT CCAGGGACGC C

21

5

(2) INFORMATION FOR SEQ ID NO: 64:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 24 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

10

(ii) MOLECULE TYPE: cDNA

15

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 64:

GCGGTAATGT GTGAAAGCGT TGCC

24

20

(2) INFORMATION FOR SEQ ID NO: 65:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 18 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

25

30

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 65:

TCCCTTGTGG CCTGTGTG

18

40

(2) INFORMATION FOR SEQ ID NO: 66:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 19 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

45

(ii) MOLECULE TYPE: cDNA

50

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 66:

TCCTTCATCG GCTCTTCGA

19

(2) INFORMATION FOR SEQ ID NO: 67:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 18 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 67:

GATGCCAAGG CATCCACC

18

(2) INFORMATION FOR SEQ ID NO: 68:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 19 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 68:

CCTCCACGT CCTTCATCG

19

(2) INFORMATION FOR SEQ ID NO: 69:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 22 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 69:

AAGGTTTCTG ACTAGTTGG GC

22

(2) INFORMATION FOR SEQ ID NO: 70:

5

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 22 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

10

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

15

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 70:

20

GGTGAAGTGC TTGCATGGAT CT

22

(2) INFORMATION FOR SEQ ID NO: 71:

25

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 23 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 71:

ACCTGTGAGT TTTCGTTCTT CTC

23

40

(2) INFORMATION FOR SEQ ID NO: 72:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 24 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

45

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

50

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 72:

55

CTATTGTTC AGTTTGTGAGA GGTT

24



(2) INFORMATION FOR SEQ ID NO: 73:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 23 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 73:

ATTTTCCGTA TCAGCGATGA TAC

23

(2) INFORMATION FOR SEQ ID NO: 74:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 22 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 74:

ACGAAGTAAA GGTGTGTTTT CT

22

(2) INFORMATION FOR SEQ ID NO: 75:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 25 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 75:

GAGAGGTTAC TCTCTTTTAT GTCAG

25

## (2) INFORMATION FOR SEQ ID NO: 76:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 275 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: cDNA

## (iii) HYPOTHETICAL: NO

## (iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 76:

AAGGAGCACC ACGAAAACGC CCCAACTGGT GGGGCGTAGG CCGTGAGGGG TTCTTGTCTG 60  
 TAGTGGGCGA GAGCCGGGTG CATGACAACA AAGTTGGCCA CCAACACACT GTTGGGTCCT 120  
 GAGGCAACAC TCGGACTTGT TCCAGGTGTT GTCCCACCGC CTTGGTGGTG GGGTGTGGTG 180  
 TTTGAGAACT GGATAGTGGT TGCAGCATC AATGGATACG CTGCCGGCTA GCGGTGGCGT 240  
 GTTCTTTGTG CAATATTCTT TGGT'TTTTGT TGTGT 275

## (2) INFORMATION FOR SEQ ID NO: 77:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 278 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: cDNA

## (iii) HYPOTHETICAL: NO

## (iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 77:

AAGGAGCACC ACGAAAAGCA CCCCAACTGG TGGGGTGCGA GCCGTGAGGG GTTCCCGTCT 60  
 GTAGTGGACG GGGGCCGGNT GCGCAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120  
 GAGACAACAC TCGGTCCGTC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT 180  
 TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCGCA TGGTCTTCGT GGCCGGCGTT 240  
 CATCGAAATG TGTAATTCT TCCTTAACTC TTGTGTGT 278

## (2) INFORMATION FOR SEQ ID NO: 78:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 278 base pairs  
 (B) TYPE: nucleic acid

(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 78:

15 AAGGAGCACC ACGAAAAGCA CCCCAACTGG TGGGGTGCGA GCCGTGAGGG GTTCCCGTCT 60  
GTAGTGACG GGGGCCGGGT GCGCAACAGC AAATGAATTG CAGACACACT ATTGGGCCCT 120  
GAGACAACAC TCGGTCCGTC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT 180  
TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCGCA TGGTCTTCGT GGCCGGCGTT 240  
20 CATCGAAATG TGAATTTCT TTTTAACTC TTGTGTGT 278

(2) INFORMATION FOR SEQ ID NO: 79:

25 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 280 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 79:

40 AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCCCGTCT 60  
GTAGTGACG GGGGCCGGNT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120  
GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT 180  
TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCGCA TAGTCCTTGT GGCTGATGCG 240  
45 CTCGTCGAAA TGTGTAATTT CTTCTTTGGT GTNTGTGTGT 280

(2) INFORMATION FOR SEQ ID NO: 80:

50 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 281 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

55 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 80:

10 AAGGAGCACC ACGAAAAGCA TCCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCTCGTCT 60  
 GTAGTGGACG AAAACCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120  
 GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT 180  
 15 TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCGCG TAGTCCTTTG TGGCTGATGC 240  
 GTTCATCAAA ATGTGTAATT TCTTTTTTGG TTTNTGTGTG T 281

(2) INFORMATION FOR SEQ ID NO: 81:

20 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 280 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 81:

35 AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCCCGTCT 60  
 GTAGTGGACG GGGGCCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120  
 GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT 180  
 40 TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCGCA TAGCCCTTGC GGCTGATGCG 240  
 TTCGNCGAAA TGTGTAATTT CTTCTCTGGT TTCTGTGTGT 280

(2) INFORMATION FOR SEQ ID NO: 82:

45 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 282 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

50 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 82:

5 AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCTCGTCT 60  
 GTAGTGGACG GNAGCCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120  
 GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT 180  
 10 TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCGCG TAGTCCTTCG TGGCTGATGC 240  
 GTTCATCGAA ATGTGTAAT TCTTCTTTGG TTTGGGTGT GT 282

## (2) INFORMATION FOR SEQ ID NO: 83:

15 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 282 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

25 (iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 83:

30 AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCCCGTCT 60  
 GTAGTGGACG GGGGCCGGGT GCACAACAGC AAATGATCGC CAGACACACT ATTGGGCCCT 120  
 GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT 180  
 35 TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCGCA TAGTCCTTTG GGGCTGATGT 240  
 GTTTCATCAA AATGTGTAAT TTCTTTTNG GTTTTNGTGT GT 282

## (2) INFORMATION FOR SEQ ID NO: 84:

40 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 281 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

50 (iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 84:

55 AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCTCGTCT 60

GTAGTGGACG GGAGCCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120  
 GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT 180  
 5 TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCGCG TAGTCCTTCG TGGCTGATGC 240  
 GTTCATTGAA ATGTGTAATT TCTTCTCTGG TTTTGTGTG T 281

## (2) INFORMATION FOR SEQ ID NO: 85:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 280 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 15 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

20 (iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 85:

25 AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCCCGTCT 60  
 GTAGTGGACG GGGGCCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120  
 GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT 180  
 30 TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCGCA TAGTCCTTGT GGCTGATCG 240  
 CTCGTCGAAA TGTGTAATTT CTTCTTTGGT TTTTGTGTG 280

## (2) INFORMATION FOR SEQ ID NO: 86:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 282 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 40 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

45 (iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 86:

50 AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCCCGTCT 60  
 GTAGTGGACG GGGGCCGGGT GCGCAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120  
 GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTTGGTGT 180  
 55 TTGAGTATTG GATAGTGGTT GCGAGCATCT AGATGAGCGC GTAGTCCTTG TGGCTGATGC 240

GTTTCGTCGAA ATGTGTAATT TCTTCTTTGG GTTTTGTGT GT

282

(2) INFORMATION FOR SEQ ID NO: 87:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 281 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 87:

AAGGAGCACC	ACGAAAAGCA	CCCCAATTGG	TGGGGTGCGA	GCCGTGAGGG	GTTCTCGTCT	60
GTAGTGGACG	GNAGCCGGNT	GCGCAACAGC	AAATGATTGC	CAGACACACT	ATTGGGCCCT	120
GAGACAACAC	TCGGNCGATC	CGTGTGGAGT	CCCTCCATCT	TGGTGGTGGG	GTGTNGTGTT	180
TGAGTATTGG	ATAGTGGTTG	CGAGCATCTA	GATGGGCGCG	TAGTCCTTTG	TGACTGATGC	240
GTTTCATCAA	ATGTGTAATT	TCTTTTGTGN	NTTNGTGTG	T		281

(2) INFORMATION FOR SEQ ID NO: 88:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 281 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 88:

AAGGAGCACC	ACGAAAAGCA	CTCCAATTGG	TGGGGTGCGA	GCCGTGAGGG	GTTCTCGTCT	60
GTAGTGGACG	GGAACCGGGT	GCACAACAGC	AAATGATTGC	CAGACACACT	ATTGGGCCCT	120
GAGACAACAC	TCGGTCGATC	CGTGTGGAGT	CCCTCCATCT	TGGTGGTGGG	GTGTGGTGTT	180
TGAGTATTGG	ATAGTGGTTG	CGAGCATCTA	GATGAGCGCA	TAGTCCTTTG	TGGCTGACGC	240
GTTTCATCGA	ATGTGTAATT	TCTTCTTTGG	TTTTTGTGTG	T		281

(2) INFORMATION FOR SEQ ID NO: 89:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 280 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 89:

AAGGAGCACC	ACGAAAAGCA	CTCCAATTGG	TGGGGTGCGA	GCCGTGANGG	GTTCCCGTCT	60
GTAGTGGACG	GGGGCCGGGT	GCACAACAGC	AAATGATTGC	CAGACACACT	ATTGGGCCCT	120
GAGACAACAC	TCGGTCGATC	CGTGTGGAGT	CCCTCCATCT	TGGTGGTGGG	GTGTGGTGTT	180
TGAGTATTGG	ATAGTGTTG	CGAGCATCTA	GATGAGCGCA	TAGTCCTTAG	GGCTGATGCG	240
TTCGTCGNAA	TGTGTAATT	CTTCTTTGGT	TTTTGTGTGT			280

(2) INFORMATION FOR SEQ ID NO: 90:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 282 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 90:

AAGGAGCACC	ACGAAAAGCA	TCCAATTGG	TGGGGTGCGA	GCCGTGAGGG	GTTCTCGTCT	60
GTAGTGGACG	AAAACCGGGT	GCACAACAGC	AAATAATTGC	CAGACACACT	ATTGGGCCCT	120
GAGACAACAC	TCGGTCGATC	CGTGTGGTGT	CCCTCCATCT	TGGTGGTGGG	GTGTGGTGTT	180
TGAGTATTGG	ATAGTGTTG	CGAGCATCTA	GATGAACGCG	TAGTCCTTCG	TGGCTGACGT	240
GTTTCATCGAA	ATGTGTAATT	TCTTNTNTTA	ACTCTTGTGT	GT		282

(2) INFORMATION FOR SEQ ID NO: 91:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 280 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear



(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 91:

```

AAGGAGCACC ACGAAAAGCA CCCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCTCGTCT    60
GTAGTGGACG GGAGCCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT    120
GAGACAACAC TCGGTCAGTC CGTGTGGTGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT    180
TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAACGCG TAGTCCTTGT GACTGACGTG    240
TTCATCGAAA TGTGTAATTT CTTTCTAAC TCTTGTGTGT    280

```

(2) INFORMATION FOR SEQ ID NO: 92:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 281 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 92:

```

AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCGA GCCGTGAGGG GTTCTCGTCT    60
GTAGTGGACG AAAGCCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT    120
GAGACAACAC TCGGTCGAAC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT    180
TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAACGCG TGGTCTTCAT GCCCGGCGTG    240
TTCATCGAAA TGTGTAATAT CTTCTCTGGT TTTCGGTGTG T    281

```

(2) INFORMATION FOR SEQ ID NO: 93:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 280 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 93:

AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCGA GCCGTGAGGG GTTCTCGTCT	60
GTAGTGGACG AAAACCGGNT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT	120
GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT	180
TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAACGCG TGGTCTTCAT GGCCGGCGTG	240
TTCATCGAAA TGTGTAATTT CTTTTNNAC TCTTGTTGT	280

(2) INFORMATION FOR SEQ ID NO: 94:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 280 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 94:

AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCGA GCCGTGAGGG GTTCTCGTCT	60
GTAGTGGACG AAAGCCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT	120
GAGACAACAC TCGGTCGAAC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT	180
TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAACGCG TGGTCTTCAT GGCCGGCGTG	240
TTCATCGAAA TGTGTAATTT CTTCTTTGGT TTTNGTGTGT	280

(2) INFORMATION FOR SEQ ID NO: 95:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 281 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 95:

AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCGA GCCGTGAGGG GTTCTCGTCT 60  
 5 GTAGTGGACG AAAACCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120  
 GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT 180  
 TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAACGCG TAGTCCTTCG NGGNCNGCGT 240  
 10 GTTCATCGAA ATGTGTAATT TCTNTTNTAA CTCTNGTGTG T 281

## (2) INFORMATION FOR SEQ ID NO: 96:

(i) SEQUENCE CHARACTERISTICS:  
 15 (A) LENGTH: 281 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA  
 20

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

25

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 96:

AAGGAGCACC ACGAAAAGCA TCCCAATTGG TGGGGTGTGA GCCGTGAGGG GTTCTCGTCT 60  
 30 GTAGTGGACG AAAACCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120  
 GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT 180  
 TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAACGCG TAGTCCTTCG GGGCCGGCGT 240  
 35 GTTCATCGAA ATGTGTAATT TCTTTTTTAA CTCTTGTGTG T 281

## (2) INFORMATION FOR SEQ ID NO: 97:

(i) SEQUENCE CHARACTERISTICS:  
 40 (A) LENGTH: 280 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA  
 45

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

50

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 97:

AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCGA GCCGTGAGGG GTTCTCGTCT 60  
 55 GTAGTGGACG AAAACCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120

EP 1 088 899 A2

5 GAGACAACAC TCGGTCGAAC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT 180  
 TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAACGCG TGGTCTTCAT GGCCGGCGTG 240  
 TTCATCGAAA TGTGTAATTT CTTCTTTAAC TCTTGTGTGT 280

(2) INFORMATION FOR SEQ ID NO: 98:

10 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 280 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 98:

25 AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCGA GCCGTGAGGG GTTCTCGTCT 60  
 GTAGTGGACG AAAACCGGGT GCACAACAGN AAATGATTGC CAGACACACT ATTGGGCCCT 120  
 GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT 180  
 TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAACGCG TGGTCTTCAT GGCCNGCGTG 240  
 TTCATCGAAA TGTGTAATTT CTTTTTTAAC TCTTGTGTGT 280

(2) INFORMATION FOR SEQ ID NO: 99:

35 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 280 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 99:

50 AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCGA GCCGTGAGGG GTTCTCGTCT 60  
 GTAGTGGACG AAAACCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120  
 GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT 180  
 TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAACGCG TGGTCTTCAT GGCCGGCGTG 240  
 TTCATCGAAA TGTGTAATTT CTTTTTTAAC TCTTGTGTGT 280

## (2) INFORMATION FOR SEQ ID NO: 100:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 281 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 100:

AAGGAGCACC ACGAAAAGCA CCCCAACTGG TGGGGTGCGA GCCGTGAGGG GTCCTCGCCT 60  
 GTAGTGGGCG GGGGCCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120  
 GAGGCAACAC TCGGCTCGTT CTGAGTGGTG TCCCTCCATC TTGGTGGTGG GGTGTGGTGT 180  
 TTGAGTATTG GATAGTGGTT GCGAGCATCT AAACGGATGC GTGGCCGGCA ACGGTGGCGT 240  
 GTTCGTTGAA ATGTGTAATT TCTTTTTTGG TTTTGTGTG T 281

## (2) INFORMATION FOR SEQ ID NO: 101:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 274 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 101:

AAGGAGCACC ACGAAAAGCA TCCCAACAAG TGGGGTGCAA NCCGTGAGGG GTTCTCGTCT 60  
 GTAGTGGACG AAAGCCGGGT GCACGACAAC AAGCAAAGCC AGACACACTA TTGGGTCCTG 120  
 AGGCAACACT CGGGCTCTGT TCGAGAGTTG TCCCACCATC TTGGTGGTGG GGTGTGGTGT 180  
 TTGAGAATTG GATAGTGGTT GCGAGCATCA AATGGATGCG TTGCCCTACG GGTAGCGTGT 240  
 TCTTTTGTGC AATTTTATTC TTTGGTTTTT GTGT 274

## (2) INFORMATION FOR SEQ ID NO: 102:

- (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 293 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

5

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

10

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 102:

15

AAGGAGCACC ATTTCCCACT CGATGAACTA GGGAAACATA AGTAGGCATC TGTACTGGAT 60

ATCTACTTGG TGAATATGTT TTGTAAATCC TGTCCACCCC GTGGATGGGT AGTCGGCAAA 120

20

ACGTCGGACT GTCATAAGAA TTGAAACGCT GGCACACTGT TGGGTCCTGA GGCAACACGT 180

TGTGTTGTCA CCCTGCTTGG TGGTGGGGTG TGGACTTTGA CTTCTGAATA GTGGTTGCGA 240

GCATCTAAAC ATAGCCTCGC TCGTTTTTGA GTGGGGCTGG TTTTGCAATT TTA 293

25

(2) INFORMATION FOR SEQ ID NO: 103:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 296 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

35

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 103:

40

AAGGAGCACC ATTTCCCACT CGGATGAACT AGGGAACATA AAGTAGGCAT CTGTAGTGGG 60

TATCTACTTG GTGAATATGT TTTGTAAATC CTGTCCACCC CCGTGGATGG GTAGTCGGCA 120

45

AAACGTCGGA CTGTCATAAG AATTGAAACG CTGGCACACT GTTGGGTCCT GAGGCAACAC 180

GTTGTGTTGT CACCCTGCTT GGTGGTGGGG TGTGGACTTT GACTTCTGAA TAGTGGTTGC 240

GAGCATCTAA ACATAGCCTC GCTCGTTTTT GAGTGAGGCT GGTTTTTGCA ATTTTA 296

50

(2) INFORMATION FOR SEQ ID NO: 104:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 274 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

55

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 104:

```

AAGGAGCACC ACGAAGAGCA CTCCAATTGG TGGGGTGCGA GCCGTGAGGG GTCATCGTCT   60
GTAGTGGACG AAGACCGGGT GCACGACAAC AAGCTAAGCC AGACACACTA TTGGGTCCTG   120
AGGCAACACC CTCGGGTGCT GTCCCCCAT CTTGGTGGTG GGGTGTGGTG TTTGAGAATT   180
GGATAGTGGT TCGGAGCATC AAAATGTATG CGTTGTCGTT CTCGGCAACG TGTTCTTTTT   240
GTGCAATTTA TTCTTTGGTT TTTGTAGTGT TTGT                274

```

(2) INFORMATION FOR SEQ ID NO: 105:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 278 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 105:

```

AAGGAGCACC ACGAAGAGCA CTCCAATTGG TGGGGTGCGA GCCGNGAGGG GTCATCGTCT   60
GTAGTGGACG AAGACTGGGT GCACGACAAC AAAGCAAGCC AGACACACTA TTGGGTCCTG   120
AGGCAACACC CTCGGGTGCT GCCCCTCCAT CTTGGTGGTG GGGTGTGGTG TTTGAGAACT   180
GGATAGTGGT TCGGAGCATC AAAAATGTAT GCGTTGTCGT TCGCGACAAC GTGTTCTTTT   240
TGTGCAATTT TAATTCTTTT GGTTTTGGTA GTGTTTGT                278

```

(2) INFORMATION FOR SEQ ID NO: 106:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 276 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 106:

AAGGAGCACC ACGAGAAGCA CTCCAATTGG TGGGGTGCAA GCCGTGAGGG GTCATCGTCT	60
GTAGTGGACG AAGACCGGGT GCACGACAAC AAGCAAAGCC AGACACACTA TTGGGTCCTG	120
10 AGGCAACACC CTCGGGTGCT GTCCCCCAT CTTGGTGGTG GGGTGTGGTG TTTGAGAACT	180
GGATAGTGGT TGCAGCATC AAAATGTATG CGTTGTCGTT CGCGGCAACG TGTCTTTTTT	240
GTGCAATTTT TATTCTTTGG TTTTGTAGT GTTTGT	276

15 (2) INFORMATION FOR SEQ ID NO: 107:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 277 base pairs
(B) TYPE: nucleic acid
20 (C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

25 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 107:

AAGGAGCACC ACGAAAAGCA CCCCAATTGG TGGGGTGCAA GCCGTGAGGG GTTCCCGCCT	60
GTAGTGGGCG GGGCCGGGTG CGCAACAGCA AATGATTGCC AGACACACTA TTGGGCCCTG	120
35 AGGCAACACT CGGATCGATT GAGTGCTTGT CCCCCATCT TGGTGGTGGG GTGTGGTGTT	180
TGAGAACTGG ATAGTGGTTG CGAGCATCTA AATGAACGCA CTGCCGATGG TGGTGTGTTC	240
GTTTTGTGTA ATTTTATCTT TTGGTTTTTG TGTGTGT	277

40 (2) INFORMATION FOR SEQ ID NO: 108:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 282 base pairs
(B) TYPE: nucleic acid
45 (C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

50 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 108:



AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGTNAGGG GTTCTCGTCT 60  
 GTAGTGGATG GCAGCCGGGT GCACANCAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120  
 GAGACAACAC TCGGTCAGTC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGNGTT 180  
 TGAGTATTGG ATAGTGGTTG CGANCATCTA GATGAACGCG TAGTCCTCNG TGGCTGACGT 240  
 GTTCATCAAA ATGTGTAATT TCTTTTANGG GTTTNGGTGT CT 282

## (2) INFORMATION FOR SEQ ID NO: 109:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 280 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: cDNA

## (iii) HYPOTHETICAL: NO

## (iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGNGAGGG GTTCTCGCCT 60  
 GTAGTGGNCG AGGGCCGGAT GCACAACAAC ACATGATTGC CAGACACACT ATTGGGCCCT 120  
 GANACAACAC TCGGCCAGTC CGTGTGGTGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT 180  
 TGAGTATNGG ATAGTNGTTG NGANCATCTA AACGGCTGCG TNGNCNNGAA CGGTGGCGTG 240  
 TTCGNTAAAA TGTGTAATTT CTTTNNNGT TTGGGTGTNT 280

## (2) INFORMATION FOR SEQ ID NO: 110:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 280 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: cDNA

## (iii) HYPOTHETICAL: NO

## (iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 110:

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCTCGCCT 60  
 GTAGTGGGCG ANGGCCGGGT GCACAACAAC AAATGATTGC CAGACACACT ATTGGGCCCT 120  
 GAGACAACAC TCGGCCAGTC CGTGTGGTGT CCCNCCATCT TGGTGGTGGG GTGTGGTGTT 180

TGAGTATTGG ATAGTGGTTG CGAGCATCTA AANGNTGCG TTGCCGNNAN CNGTGGCGTN 240  
 5 TTCGNTAAAA TGTGTAANTT CTTTTTNGGT TTGTGTGTGT 280

(2) INFORMATION FOR SEQ ID NO: 111:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 471 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 111:

ATCGAAGATC CCGGCTTCTT CATAAGCTCC CACACGAATT GCTTGATTCA CTGGTTAGAC 60  
 25 GATTGGGTCT GTAGCTCAGT TGGTTAGAGC GCACCCCTGA TAAGGGTGAG GTCGGCAGTT 120  
 CGAATCTGCC CAGACCCACC AATTGTTGGT GTGCTGCGTG ATCCGATACG GGGCCATAGC 180  
 TCAGCTGGGA GAGCGCCTGC TTGACGCA GGAGGTCAGG AGTTCGATCC TCCTTGGCTC 240  
 30 CACCATCTAA AACAACTGTC GAAAGCTCAG AAATGAATGT TCGTGGATGA ACATTGATTT 300  
 CTGGTCTTTG CACCAGAACT GTTCTTTAAA AATTCGGGTA TGTGATAGAA GTAAGACTGA 360  
 ATGATCTCTT TCACTGGTGA TCATTCAAGT CAAGGTAAAA TTTGCGAGTT CAAGCGCGAA 420  
 35 TTTTCGGCGA ATGTCGTCTT CACAGTATAA CCAGATTGCT TGGGGTTATA T 471

(2) INFORMATION FOR SEQ ID NO: 112:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 520 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 112:

ATCGAAGACA TCAGCTTCTT CATAAGTATC CACACGAATT GCTTGATTCA TAGTCGAACG 60  
 55 AATGCTGTAA CGCGACCCGT GTTATAGGTC TGTAGCTCAG TTGGTTAGAG CGCACCCCTG 120

ATAAGGGTGA GGTCCGCAGT TCAAATCTGC CCAGACCTAC CAATTGCTTG GTCGAGAAGA 180  
 ATACGGGGCC ATAGCTCAGC TGGGAGAGCG CCTGCCTTGC ACGCAGGAGG TCAGCGGTTC 240  
 5 GATCCCGCTT GGCTCCACCA CTCTCTCGTG TTGCGGTGAG TGTTAAAGAG TTCAGAAATG 300  
 ATGCCGCTTC AGGTTTGTCC TGTGAGTGC TGATTCTGG TCTTTTGACC GGTACGAAAA 360  
 TCGTTCTTTA AAAATTTGGA TATGTGATAG AAGTGACTGA TTAATTGCTT TCACTGGCAA 420  
 10 TTGATCTGGT CAAGGTAAAA TTTGTAGTTC TCAAGACGCA AATTTTCGGC GAATGTCGTC 480  
 TTCACGATTG AGACAGTAAC CAGATTGCTT GGGGTTATAT 520

(2) INFORMATION FOR SEQ ID NO: 113:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 504 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 113:

ATCGAAGACA CCGGCTTCGT CATAAGCTCC CACACGAATT GCTTGATTCA CTTGCGAAAG 60  
 GCGATTGGGT TTAGACCCGA GAGTAACGAT TGGGTCTGTA GCTCAGTTGG TTAGAGCGCA 120  
 CCCCTGATAA GGGTGAGGTC GGCAGTTCGA ATCTGCCAG ACCCACCAAT CGAAGGGGCC 180  
 35 ATAGCTCAGC TGGGAGAGCG CCTGCTTTCG ACGCAGGAGG TCAGCGGTTC GATCCCGCTT 240  
 GGCTCCACCA TTAAGTCTAG TCGCCGAAAG CTCAGAAATG AGTGTTTACC AGGATGAGGT 300  
 40 TGATTGCCTG GGTGAACAT TGATTCTGG ACTTTGCCG AGAACTGTTC TTTAAAAATT 360  
 TGGGTATGTG ATAGAAGTAG ACCGATGTGT TGCTTTCCT GGCAGCATGT CGCGTCAAGG 420  
 TAAAATTGTC GTGTTCTCTA TGCAAATTTT CGGCGAATGT CGTCTTCACG TTATAGACAG 480  
 45 TAACCAGATT GCTTGGGGTT ATAT 504

(2) INFORMATION FOR SEQ ID NO: 114:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 499 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 114:

ATCGAAGACT TCAGCTTCTT CATAAGTTCC CACACGAATT GCTTGATTCA CTTGCGAAAA 60  
 10 GCGATTGGGT TGAGACCCGA GAGTGACGAT TGGGTCTGTA GCTCAGTTGG TTAGAGCGCA 120  
 CCCCTGATAA GGGTGAGGTC GGCAGTTCGA ATCTGCCAG ACCCACCAAT TGTCGGGATG 180  
 GCCAGTGTCA AATGGGGCCA TAGCTCAGCT GGGAGAGCGC CTGCTTTGCA CGCAGGAGGT 240  
 15 CAGGAGITCG ATCCTCCTTG GCTCCACCAT CAACTCACGA TCGCTGAAAG CTCAGAAATG 300  
 AACATTGGTA GTTCAATGTT GATTCTCGGT CTTTGCGCCA GAACTGTTCT TAAAAAATTT 360  
 GGGTATGTGA TAGAAGTGAC TAACAGCGTG TTTCAGTGA CGTTGTTAAT CAAGGCAAAA 420  
 20 TTTGCGAGTT CAAGCGCGAA TTTTCGGCGA ATGTCGTCTT CACGTTACGA ATCTATAACC 480  
 AGATTGCTTG GGGTTATAT 499

25 (2) INFORMATION FOR SEQ ID NO: 115:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 468 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 30 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

35

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 115:

40 ATCGACGACA TCAGCTGTCT CATAAGCTCC CACACGAATT GCTTGATTCA TTGAAGAAGA 60  
 CGATTAGGTT AGCAACCTTC GATTGGGTCT GTAGCTCAGT TGGTTAGAGC GCACCCCTGA 120  
 TAAGGGTGAG GTCGGCAGTT CGAATCTGCC CAGACCCACC AATTTGCTGG GGCCATAGCT 180  
 45 CAGCTGGGAG AGCGCCTGCC TTGCACGCAG GAGGTCAGCG GTTCGATCCC GCTTGGCTCC 240  
 ACCACCCCGC TTGCCAGTTT GTCAAAGCTT AGAAATGAAT ATTCGCGTCG AATATTGATT 300  
 TCTGAACTTT ATCAGAATCG TTCTTTAAAA ATTTGGGTAT GTGATAGAAA GATAGACTGG 360  
 50 ACAGCACTTT CACTGGTGTG TGTTTCAGGCT AAGGTAAAAT TTGTGAGTAA TTACAAGTTT 420  
 TCGGCGAATG TTGTCTTCAC AGTATAACCA GATTGCTTGG GGTATAT 468

55

(2) INFORMATION FOR SEQ ID NO: 116:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 246 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 116:

TAAGGAAAAG GAAACCTGTG AGTTTTCGTT CTTCTCTGTT TGTTCAGTTT TGAGAGGTTA	60
ATTCTTCTCT ATACTGTTTG TTCTTTGAAA ACTAGATAAG AAAGTTACTA AAGTTAGCAT	120
AAATAGGTAA CTATTTATGA CACAAGTAAC CGAGAATCAT CTGAAAGTGA ATCTTTCATC	180
TGATTGGAAG TATCATCGCT GATACGAAAA ATCAGAAAAA CAACCTTTAC TTCATCGAAG	240
TAAATT	246

(2) INFORMATION FOR SEQ ID NO: 117:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 246 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 117:

CTAAGGAAAA GGAAACCTGT GAGTTTTCGT TCTTCTCTAT TTGTTTCAGTT TTGAGAGGTT	60
AGTACTTCTC AGTATGTTTG TTCTTTGAAA ACTAGATAAG AAAGTTAGTA AAGTTAGCAT	120
AGATAATTTA TTATTTATGA CACAAGTAAC CGAGAATCAT CTGAAAGTGA ATCTTTCATC	180
TGATTGGAAG TATCATCGCT GATACGAAAA ATCAGAAAAA CAACCTTTAC TTCGTAGAAG	240
TAAATT	246

(2) INFORMATION FOR SEQ ID NO: 118:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 246 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

5 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 118:

TAAGGAAAAG	GAAACCTGTG	AGTTTTCGTT	CTTCTCTGTT	TGTTCAAGTTT	TGAGAGGTTA	60
TTACTTCTCT	GTATGTTTGT	TCTTTGAAAA	CTAGATAAGA	AAGTTAGTAA	AGTTAGCATA	120
15 AGTAGTGTA	CTATTTATGA	CACAAGTAAC	CGAGAATCAT	CTGAAAGTGA	ATCTTTCATC	180
TAATTCGACG	TATCATCGCT	GATACAGACA	ATTAGAAAAA	CAACCTTTAC	TTCGACGAAG	240
20 TAAATT						246

(2) INFORMATION FOR SEQ ID NO: 119:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 363 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

25

(ii) MOLECULE TYPE: cDNA

30

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 119:

GGCCTATAGC	TCAGCTGGTT	AGAGCGCACG	CCTGATAAGC	GTGAGGTCGA	TGGTTCGAGT	60
CCATTTAGGC	CCACTTTTTC	TTTCTGACAG	AAGAAACACT	GTATAACCTA	TTTAAGGGGC	120
40 CTTAGCTCAG	CTGGGAGAGC	GCCTGCTTTG	CACGCAGGAG	GTCAGCGGTT	CGATCCCGCT	180
AGGCTCCACC	AAAATTGTTC	TTTGAAAAC	AGATAAGAAA	GTTAGTAAAG	TTAGCATAAA	240
45 TAGGTAACTA	TTTATGACAC	AAGTAACCGA	GAATCATCTG	AAAGTGAATC	TTTCATCTGA	300
TTGGAAGTAT	CATCGCTGAT	ACGAAAAATC	AGAAAAACAA	CCTTTACTTC	ATCGAAGTAA	360
ATT						363

50

(2) INFORMATION FOR SEQ ID NO: 120:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 496 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

55

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 120:

TAAGGAAAAG	GAAACCTGTG	AGTTTTCGTT	CTTCTCTATT	TGTTTCAGTTT	TGAGAGGTTA	60
CTCTCTTTTA	TGTCAGATAA	AGTATGCAAG	GCACTATGCT	TGAAGCATCG	CGCCACTACA	120
TTTTTGACGG	GCCTATAGCT	CAGCTGGTTA	GAGCGCACGC	CTGATAAGCG	TGAGGTCGAT	180
GGTTCGAGTC	CATTTAGGCC	CAC TTTTCT	TTCTGACATA	AGAAATACAA	ATAATCATAC	240
CCTTTTACGG	GGCCTTAGCT	CAGCTGGGAG	AGCGCCTGCT	TTGCACGCAG	GAGGTCAGCG	300
GTTTCGATCCC	GCTAGGCTCC	ACCAAAATTG	TTCTTTGAAA	ACTAGATAAG	AAAGTTAGTA	360
AAGTTAGCAT	AGATAATTTA	TTATTTATGA	CACAAGTAAC	CGAGAATCAT	CTGAAAGTGA	420
ATCTTTCATC	TGATTGGAAG	TATCATCGCT	GATACGGAAA	ATCAGAAAAA	CAACCTTTAC	480
TTCGTAGAAG	TAAATT					496

(2) INFORMATION FOR SEQ ID NO: 121:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 498 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 121:

TAAGGAAAAG	GAAACCTGTN	AGTTTNCGTN	CTTCTCTGTT	TGTNCAGTTT	TNAGAGGTTA	60
CTCTCTTTNA	TGTCAGATAA	AGTACGCACG	GCACGTTGCC	TTGGGCAAAG	AGCCACTACA	120
TTATTGACGG	GCCTATAGCT	CAGCTGGTTA	GAGCGCACGC	CTGATAAGCG	TGAGGTCGAT	180
GGTTCGAGTC	CATTTAGGCC	CAC TTTTCT	TTCTGACAGA	AGAAATCATT	TGCACATCCT	240
ATTAATAAGG	GNCCTTAGCT	CAGCTGGGAG	AGCGCCTGCT	TTGCACGCAG	GAGGTCAGCG	300
GTTTCGATCCC	GCTAGGCTCC	ACCCAAAATT	GTTCTTTGAA	AACTAGATAA	GAAAGTTAGT	360
AAAGTTAGCA	TAAGTAGTAT	AACTATTTAT	GACACAAGTA	ACCGAGAATC	ATCTGAAAGT	420
GAATCTTTCA	TCTAATTCGA	CGTATCATCG	CTGATACAGA	CAATTNGAAA	AACAACCTTT	480

ACTTCGACGA AGTAAATT

498

5 (2) INFORMATION FOR SEQ ID NO: 122:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 229 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

10

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

15

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 122:

20

TAAGGATAAG GATAACTGTC TTAGGACGGT TTGACTAGGT TGGGCAAGCG TTTTTTTAAT 60

CTTGTATTCT ATTCCTTTTG CATTTGTTAAG CGTTGTTCC AAAACATTTA GTTTACGATC 120

25

AAGTATGTTA TGTAATAAT ATGTAACAA GTAAATTCAC ATATAATAAT AGACGTTTAA 180

GAATATATGT CTTTAGGTGA TGTTAACTTG CATGGATCAA TAATTTACA 229

(2) INFORMATION FOR SEQ ID NO: 123:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 248 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 123:

45 TAAGGATAAG GAAGAAGCCT GAGAAGGTTT CTGACTAGGT TGGGCAAGCA TTTATATGTA 60

AGAGCAAGCA TTCTATTTC A TTTGTGTTGT TAAGAGTAGC GTGGTGAGGA CGAGACATAT 120

AGTTTGTGAT CAAGTATGTT ATTGTAAAGA AATAATCATG GTAACAAGTA TATTTACGCG 180

50

ATAATAATAG ACGTTTAAAGA GTATTTGTCT TTTAGGTGAA GTGCTTGCAT GGATCTATAG 240

AAATTACA 248

(2) INFORMATION FOR SEQ ID NO: 124:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 224 base pairs

55



(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 118:

TAAGGAAAAG GAAACCTGTG AGTTTTCGTT CTTCTCTGTT TGTTCAAGTTT TGAGAGGTTA	60
TTACTTCTCT GTATGTTTGT TCTTTGAAAA CTAGATAAGA AAGTTAGTAA AGTTAGCATA	120
AGTAGTGTA CTATTTATGA CACAAGTAAC CGAGAATCAT CTGAAAGTGA ATCTTTCATC	180
TAATTCGACG TATCATCGCT GATACAGACA ATTAGAAAAA CAACCTTTAC TTCGACGAAG	240
TAAATT	246

(2) INFORMATION FOR SEQ ID NO: 119:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 363 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 119:

GGCCTATAGC TCAGCTGGTT AGAGCGCACG CCTGATAAGC GTGAGGTCGA TGGTTCGAGT	60
CCATTTAGGC CCACTTTTTC TTTCTGACAG AAGAAACACT GTATAACCTA TTTAAGGGGC	120
CTTAGCTCAG CTGGGAGAGC GCCTGCTTTG CACGCAGGAG GTCAGCGGTT CGATCCCGCT	180
AGGCTCCACC AAAATTGTTT TTTGAAAACCT AGATAAGAAA GTTAGTAAAG TTAGCATAAA	240
TAGGTAAC TA TTTATGACAC AAGTAACCGA GAATCATCTG AAAGTGAATC TTTCATCTGA	300
TTGGAAGTAT CATCGCTGAT ACGAAAAATC AGAAAAACAA CCTTTACTTC ATCGAAGTAA	360
ATT	363

(2) INFORMATION FOR SEQ ID NO: 120:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 496 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 120:

```

5      TAAGGAAAAG GAAACCTGTG AGTTTTCGTT CTTCTCTATT TGTTCAGTTT TGAGAGGTTA      60
      CTCTCTTTTA TGTCAGATAA AGTATGCAAG GCACTATGCT TGAAGCATCG CGCCACTACA      120
15     TTTTGTACGG GCCTATAGCT CAGCTGGTTA GAGCGCACGC CTGATAAGCG TGAGGTCGAT      180
      GGTTTCGAGTC CATTTAGGCC CACTTTTTCT TTCTGACATA AGAAATACAA ATAATCATAC      240
      CCTTTTACGG GGCCTTAGCT CAGCTGGGAG AGCGCCTGCT TTGCACGCAG GAGGTCAGCG      300
20     GTTCGATCCC GCTAGGCTCC ACCAAAATTG TTCTTTGAAA ACTAGATAAG AAAGTTAGTA      360
      AAGTTAGCAT AGATAATTTA TTATTTATGA CACAAGTAAC CGAGAATCAT CTGAAAGTGA      420
      ATCTTTCATC TGATTGGAAG TATCATCGCT GATACGAAA ATCAGAAAAA CAACCTTTAC      480
25     TTCGTAGAAG TAAATT                                     496

```

(2) INFORMATION FOR SEQ ID NO: 121:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 498 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 121:

```

45     TAAGGAAAAG GAAACCTGTN AGTTTNCGTN CTTCTCTGTT TGTNCAGTTT TNAGAGGTTA      60
      CTCTCTTTNA TGTCAGATAA AGTACGCACG GCACGTTGCC TTGGGCAAAG AGCCACTACA      120
      TTATTGACGG GCCTATAGCT CAGCTGGTTA GAGCGCACGC CTGATAAGCG TGAGGTCGAT      180
      GGTTTCGAGTC CATTTAGGCC CACTTTTTCT TTCTGACAGA AGAAATCATT TGCACATCCT      240
50     ATTAATAAGG GNCCTTAGCT CAGCTGGGAG AGCGCCTGCT TTGCACGCAG GAGGTCAGCG      300
      GTTCGATCCC GCTAGGCTCC ACCCAAATT GTTCTTTGAA AACTAGATAA GAAAGTTAGT      360
      AAAGTTAGCA TAAGTAGTAT AACTATTTAT GACACAAGTA ACCGAGAATC ATCTGAAAGT      420
55     GAATCTTTCA TCTAATTCGA CGTATCATCG CTGATACAGA CAATTNGAAA AACACCTTT      480

```

ACTTCGACGA AGTAAATT

498

## 5 (2) INFORMATION FOR SEQ ID NO: 122:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 229 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

10

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

15

(iii) ANTI-SENSE: NO

20

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 122:

TAAGGATAAG GATAACTGTC TTAGGACGGT TTGACTAGGT TGGGCAAGCG TTTTTTAAAT	60
CTTGTATTCT ATTCTTTTG CATTGTAAAG CGTTGTTTCC AAAACATTTA GTTTACGATC	120
AAGTATGTTA TGTAATAAT ATGGAACAA GTAAATTCAC ATATAATAAT AGACGTTTAA	180
GAATATATGT CTTAGGTGA TGTTAACTTG CATGGATCAA TAATTTACA	229

25

## (2) INFORMATION FOR SEQ ID NO: 123:

30

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 248 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

35

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

40

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 123:

TAAGGATAAG GAAGAAGCCT GAGAAGGTTT CTGACTAGGT TGGGCAAGCA TTTATATGTA	60
AGAGCAAGCA TTCTATTTCA TTTGTGTTGT TAAGAGTAGC GTGGTGAGGA CGAGACATAT	120
AGTTTGTGAT CAAGTATGTT ATTGTAAAGA AATAATCATG GTAACAAGTA TATTTACGCG	180
ATAATAATAG ACGTTTAAAG GATTGTTCT TTTAGGTGAA GTGCTTGCAT GGATCTATAG	240
AAATTACA	248

45

50

## (2) INFORMATION FOR SEQ ID NO: 124:

55

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 224 base pairs

(B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

5

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

10

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 124:

15

CAAATGGAGT TTTTATTTTT TATTTATCTT AAACACCCAT TAATTTTTTC GGTGTTAAAA 60

CCCAAATCAA TGTTTGGTCT CACAATAAC ACATTTGGTC AGTTTGTATC CAGTTCTGAA 120

AGAATGTTTT TGAACAGTTC TTTCAAAAC GAAAACGACA ATCTTTCTAG TTCCAAAAAT 180

20

AAATACAAA GGATCAATAC AATAAGTTAC TAAGGGCTTA TGGT 224

(2) INFORMATION FOR SEQ ID NO: 125:

25

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 252 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 125:

40

CTAATGAAGT TTTTACTTTT TTCTTTTCAT CTTTAATAAA GATAAATACT AAACAAAACA 60

TCAAAATCCA TTTATTTATC GGTGGTAAAT TAAACCCAAA TCCCTGTTTG GTCTCACAAC 120

TAAATATTT GGTGAGATTG TATCCAGTTC TGAAAGAACA TTTCCGCTTC TTTCAAAAC 180

45

GAAAACGACA ATCTTTCTAG TTCCAAATAA ATACCAAAGG ATCAATACAA TAAGTTACTA 240

AGGGCTTATG GT 252

(2) INFORMATION FOR SEQ ID NO: 126:

50

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 608 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

55

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 126:

10	AACGAAAGAT TGACGATTGG TAAGAATCCA CAACAAGTTG TTCTTCATAG ATGTATCTGA	60
	GGGTCTGTAG CTCAGTTGGT TAGAGCACAC GCTTGATAAG CGTGGGGTCA CAAGTTCAAG	120
	TCTTGTCAGA CCCACCATGA CTTTGACTGG TTGAAGTTAT AGATAAAGA TACATGATTG	180
15	ATGATGTAAG CTGGGGACTT AGCTTAGTTG GTAGAGCGCC TGCTTTGCAC GCAGGAGGTC	240
	AGGAGTTCGA CTCTCCTAGT CTCCACCAGA ACTTAAGATA AGTTCGGATT ACAGAAATTA	300
	GTAAATAAAG ATTGAGATCT TGGTTTATTA ACTTCTGTGA TTTTATTATC ACGGTAATTA	360
20	GTGTGATCTG ACGAAGACAC ATTAATCAT TAACAGATTG GCAAAATTGA GTCTGAAATA	420
	AATTGTTTAC TCAAGAGTTT AGGTTAAGCA ATTAATCTAG ATGAATTGAG AACTAGCAAA	480
	TTAACTGAAT CAAGCGTTTT GGTATGTGAA TTTAGATTGA AGCTGTACAG TGCTTAAGTG	540
25	CACAGTGCTC TAAACTGAAA TGTTGAAGTT ACTAACTTGT AGGTAACATC GACTGTTTGG	600
	GGTTGTAT	608

(2) INFORMATION FOR SEQ ID NO: 127:

30

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 269 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

35

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

40

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 127:

45	AACGAAAGAT TGACGATTGG TAAGAATCCA CGACAAGTTG TTCTTCATAG ATGTATCTGA	60
	GGGTCTGTAG CTCAGTTGGT TAGAGCACAC GCTTGATAAG CGTGGGGTCA CAAGTTCAAG	120
	TCTTGTCAGA CCCACCATGA CTTTGACTGG TTGAAGTTAT AGAAAAGAAG ATACATAACT	180
50	GATGATGTAA GCTGGGGACT TAGCTTAGTT GGTAGAGCGC CTGCTTTGCA CGCAGGAGGT	240
	CAGGAGTTCG ACTCTCCTAG TCTCCACCA	269

(2) INFORMATION FOR SEQ ID NO: 128:

55

- (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 249 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

5

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

10

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 128:

15

AACGAAAGAT TGATGGCCGG TAAGAATCCA CAACAAGTTG TTCTTCGAAG ATGTATCTGA	60
GGGTCTGTAG CTCAGTTGGT TAGAGCACAC GCTTGATAAG CGTGGGGTCA CAAGTTCAAG	120
TCTTGTCAGA CCCACCAAAT CTGAAAGATA TGTCGTTTAT TATGATTAAA GCTGGGGACT	180
TAGCTTAGTT GGTAGAGCGC CTGCTTTGCA CGCAGGAGGT CAGGAGTTCT ACTCTCCTAG	240
TCTCCACCA	249

20

25

(2) INFORMATION FOR SEQ ID NO: 129:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 283 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

35

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 129:

40

AACGAAAGAT TGACGATTGG TAAGAATCCA CAACAAGTTG TTCTTCATGA CGATGTATCT	60
GAGGGTCTGT AGCTCAGTTG GTTAGAGCAC ACGCTTGATA AGCGTGGGGT CACAAGTTCA	120
AGTCTTGTC A GACCCACCAA ATCTGACTAA CAAGCATTAT TAAATGCTGA ATACAGAAAA	180
ACAGAGACAT TGACTTATTG ATAAGCTGGG GACTTAGCTT AGTTGGTAGA GCGCCTGCTT	240
TGCACGCAGG AGGTCAGGAG TTCGACTCTC CTAGTCTCCA CCA	283

45

50

(2) INFORMATION FOR SEQ ID NO: 130:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 283 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

55

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 130:

```

AACGAAAGAT TGGTGACCGG TAAGAATCCA CAACAAGTTG TTCTTCGAAG ATGTATCTGA      60
GGGTCTGTAG CTCAGTTGGT TAGAGCACAC GCTTGATAAG CGTGGGGTCA CAAGTTCAAG      120
TCTTGTCAGA CCCACCACTA CTGACGAAGT GATGAATAAT CACAAGCTGC TAGATGAAAA      180
GATATGTCGT TCATTATGAT TAAAGCTGGG GACTTAGCTT AGTTGGTAGA GCGCCTGCTT      240
TGCACGCAGG AGGTCAGGAG TTCGACTCTC CTAGTCTCCA CCA                        283

```

(2) INFORMATION FOR SEQ ID NO: 131:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 808 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 131:

```

TAAGGAAGAT CGAGAATTGG AAAGAGGTCG GATTTATCCG GATGATCCTT CTCCATCTTA      60
TTAGAACATA GATCGCAGGC CAGTCAGCCT GACGATCGCT TGCAGGCGTG CCGCCTTCGT      120
TTCTCTTTCT TCATTGTTGA TTGCTCACGG GCCGTACCGC AGCTGACGCT GCTGGCCCTG      180
CGCAGGCGCG GCCCATCAGG GCCGACGGCC GGTGGGCCTT GCNAAGCTTC GCTTCGGGGT      240
GGATCTGTGG ATCGCGTAGT AGCGTTTGCG TCGGTATCTG GGCTTGTAGC TCAGTTGGTT      300
AGAGCACACG CTTGATAAGC GTGGGGTCGG AGGTTCAAGT CCTCCCAGGC CCACCAAGTT      360
ACTTGATGAG GGGCCGTAGC TCAGCTGGGA GAGCACCTGC TTTGCAAGCA GGGGGTCGTC      420
GGTTCGATCC CGTCCGGCTC CACCATCATG TTGGTGTGTA GACGGATATT GGCAATCAAC      480
AAAAGAAAGA AACAAGTTTG CGGACTNTTA CGAAAGTCTG CCTGTTCTGT ATGAAATCGT      540
GAAGAGAAGA TGTAATCGGA TCAACTGAAG AGTTGATGTC GCAAGAAGCT TGCTCAAGCC      600
TTGCATAATG ATTGATGTGT TTAACGCCA TCACCGATTG TATCTCGAGA AGCTGGTCTT      660
TCTGCTGATA CTGTTGAAAC GAGCATTGTC AGTCGAATGG CAACATTCGG CGTCGCATAA      720

```

TGCGGCTTTA AGAGCTGAGT TTTGATGGAT ATTGGCAATG AGAGTGATCA AGTGTCTTAA 780  
 5 GGGCATTGGT GGATGCCTTG GCATGCAC 808

(2) INFORMATION FOR SEQ ID NO: 132:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 808 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 132:

TAAGGAGGAT CGAGAATTGG AAAGAGGCCG GATTTATCCG GATGATCCTT CTCCATCTTA 60  
 25 TTAGAACATA GATCGCAGNC CAGTCAGCCT GACGATCGCT TGCAGGCGTG CCGCCTTCGT 120  
 TTCTCTTTCT TCATTGTTGA TTGCTCACGG GCCGTACCGC AGCTGACGCT GCTGGCCCTG 180  
 CGCAGGCGCG GNCCATCAGG GCCGACGGCC GGTGGCCTT GCGAAGCTTC GCTTCGGGGT 240  
 30 GGATCTGTGG ATCGCGTAGT AGCGTTTGGC TCGGTATCTG GGCTTGTAGC TCAGTTGGTT 300  
 AGAGCACACG CTTGATAAGC GTGGGGTCGG AGGTTCAAGT CCTCCCAGGC CCACCAAGTT 360  
 ACTTGATGAG GGGCCGTAGC TCAGCTGGGA GAGCACCTGC TTTGCAAGCA GGGGGTCGTC 420  
 35 GGTTCGATCC CGTCCGGCTC CACCATCATG TTGGTGTGA GACGGATATT GGCAATCAAC 480  
 AAAAGAAAGA AACAAGTTTG CGGACTNTTA CGAAAGTCTG CCTGTTCTGT ATGAAATCGT 540  
 GAAGAGAAGA TGTAATCGGA TCAACTGAAG AGTTGATGTC GCAAGAAGCT TGCTCAAGCC 600  
 40 TTGCATAATG ATTGATGTGT TTAACCGCCA TCACCGATTG TATCTCGAGA AGCTGGTCTT 660  
 TCTGCTGATA CTGTTGAAAC GAGCATTTGC AGTCGAATGG CAACATTCGG CGTCGCATAA 720  
 45 TGCGGCTTTA AGAGCTGAGT TTTGATGGAT ATTGGCAATG AGAGTGATCA AGTGTCTTAA 780  
 GGGCATTGGT GGATGCCTTG GCATGCAC 808

(2) INFORMATION FOR SEQ ID NO: 133:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 353 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA



(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 133:

CCTTAAAGAA CTGTTCTTTG CAGTGCTCAC ACAGATTGTC TGATGAAAAG TAAATAGCAA	60
GGCGTCTTGC GAAGCAGACT GATACGTCCTTCTCGTCTAG AGGCCAGGA CACCGCCCTT	120
TCACGGCGGT AACAGGGGT CGAATCCCCT AGGGGACGCC ACTTGCGCGG TAATGTGTGA	180
AAGCGTTGCC ATCAGTATCT CAAACTGAC TTACGAGTCA CGTTTGAGAT ATTTGCTCTT	240
TAAAAATCTG GATCAAGCTG AAAATTGAAA CACAGAACAA CGAAAGTTGT TCGTGAGTCT	300
CTCAAATTTT CGCAACACGA TGATGAATCG TAAGAAACAT CTTCGGGTTG TGA	353

(2) INFORMATION FOR SEQ ID NO: 134:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 515 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 134:

CCTTAAAGAA CTGTTCTTTG CAGTGCTCAC ACAGATTGTC TGATGAAAAA CGAGCAGTAA	60
AACCTCTACA GGCTTGAGC TCAGGTGGTT AGAGCGCACC CCTGATAAGG GTGAGGTCGG	120
TGTTCAAGT CCACTCAGGC CTACCAAATT TTCCCTGAAT ACTGCGTTGT GAAATAACTC	180
ACATACTGAT GTATGCTTCG TTATCCACG CCTTGCTCTCA GGAAAAATTA TCGGTAAAGA	240
GGTCTGACT ACACGATGGG GCTATAGCTC AGCTGGGAGA GCGCCTGCTT TGCACGCAGG	300
AGGTCTGCGG TTCGATCCCG CATAGCTCCA CCATATCGTG AGTGTTTACG AAAAAATACT	360
TCAGAGTGTA CCTGAAAGGG TCACTGCGA AGTTTGTCTC TTAAAAATC TGGATCAAGC	420
TGAAAATTGA AACACAGAAC AACGAAAGTT GTTCGTGAGT CTCTCAAATT TTCGCAACAC	480
GATGATGAAT CGTAAGAAAC ATCTTCGGGT TGTGA	515

(2) INFORMATION FOR SEQ ID NO: 135:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 353 base pairs  
 (B) TYPE: nucleic acid

(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 135:

CCTTAAAGAA	CGCTACTTTG	CAGTGCTCAC	ACAGATTGTC	TGATGAAAAG	TAAATAGCAA	60
15	GGCGTCTTGC	GAAGCAGACT	GATACGTCCC	CTTCGTCTAG	AGGCCCAGGA	120
	TCACGGCGGT	AACAGGGGTT	CGAATCCCCT	AGGGGACGCC	ACTTGCGCGG	180
	AAGCGTTGCC	ATCAGTATCT	CAAACTGAC	TTACGAGTCA	CGTTTGAGAT	240
20	TAAAAATCTG	GATCAAGCTG	AAAATTGAAA	CACAGAACAA	CGAAAGTTGT	300
	CTCAAATTTT	CGCAACACGA	TGATGAATCG	TAAGAAACAT	CTTCGGGTTG	353

25 (2) INFORMATION FOR SEQ ID NO: 136:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 481 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 30 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

35 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 136:

40	CCTTAAAGAA	CTGTTCTTTG	AAGTGCTCAC	ACAGATTGTC	TGATGAAAAA	CGAGCAGTAA	60
	AACCTCTACA	GGCTTGTAGC	TCAGGTGGTT	AGAGCGCACC	CCTGATAAGG	GTGAGGTCGG	120
	TGGTTCAAGT	CCACTCAGGC	CTACCAAATT	TTCCCTGAAT	ACTGCGTTGT	GAAATAACTC	180
45	ACATACTGAT	GTATGCTTCG	TTATTCCACG	CCTTGTCTCA	GGAAAAATTA	TCGGTAAAGA	240
	GGTTCTGACT	ACACGATGGG	GCTATAGCTC	AGCTGGGAGA	GCGCCTGCTT	TGCACGCAGG	300
	AGGTCTGCGG	TTCGATCCCG	CATAGCTCCA	CCATCTCGTG	AGTGTTTACG	AAAAAATACT	360
50	TCAGAGTGTA	CCTGAAAGGG	TTCAGTCCGA	AGTTTTGCTC	TTTAAAAATC	TGGATCAAGC	420
	TGAAAATTGA	AACACAGAAC	AACGAAAGTT	GTTCTGTGAGT	CTCTCAAATT	TTCGCAACAC	480
55	G						481

## (2) INFORMATION FOR SEQ ID NO: 137:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 392 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: cDNA

## (iii) HYPOTHETICAL: NO

## (iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 137:

CCTTAAAGAA GCGTACTTTG AAGTGCTCAC ACAGATTGTC TGATGAAAAG TGAATAGCAA 60  
 GGCGTCTTGC GATTGAGACT TCAGTGTCCTT CTTCGTCTAG AGGCCAGGA CACCGCCCTT 120  
 TCACGGCGGT AACAGGGGTT CGAATCCCCT AGGGGACGCC AGCGTTCAAA CTGATGAGGT 180  
 CAAACCTCCA GGGACGCCAC TTGCTGGTTT GTGAGTGAAA GTCACCTGCC TTAATATCTC 240  
 AAAACTGACT TACGAGTCAC GTTTGAGATA TTTGCTCTTT AAAAATCTGG ATCAAGCTGA 300  
 AAATTGAAAC ACAGAACAAC GAAAGTTGTT CGTGAGTCTC TCAAATTTTC GCAACACGAT 360  
 GATGAATCGT AAGAAACATC TTCGGGTTGT GA 392

## (2) INFORMATION FOR SEQ ID NO: 138:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 515 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: cDNA

## (iii) HYPOTHETICAL: NO

## (iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 138:

CCTTAAAGAA ACGGTCTTTG AAGTGCTCAC ACAGATTGTC TGATGAAAAA CGAGCAGTAA 60  
 AACCTCTACA GGCTGTAGC TCAGGTGGTT AGAGCGCACC CCTGATAAGG GTGAGGTCGG 120  
 TGGTCAAGT CCACTCAGGC CTACCAAATT TTCCTGAAT ACTGCGTTGT GAAATAACTC 180  
 ACATACTGAT GTATGCTTCG TTATTCCACG CCTGTCTCA GGAAAAATTA TCGGTAAAGA 240  
 GGTCTGACT ACACGATGGG GCTATAGCTC AGCTGGGAGA GCGCCTGCTT TGCACGCAGG 300  
 AGGTCTGCGG TTCGATCCCG CATAGCTCCA CCATCTCGTG AGTGTTTACG AAAAAATACT 360

TCAGAGTGTA CCTGAAAGGG TTCACTGCGA AGTTTTGCTC TTAAAAATC TGGATCAAGC 420  
 5 TGA AAAATTGA AACACAGAAC AACGAAAGTT GTTCGTGAGT CTCTCAAATT TTCGCAACAC 480  
 GATGATGAAT CGTAAGAAAC ATCTTCGGGT TGTGA 515

## (2) INFORMATION FOR SEQ ID NO: 139:

10 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 365 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

20 (iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 139:

25 CTAAGGATAT ATTCGGAACA TCTTCTTCGG AAGATGCGGA ATAACGTGAC ATATTGTATT 60  
 CAGTTTTGAA TGTTTATTTA ACATTCAAAT ATTTTTTGGT TAAAGTGATA TTGCTTTTGA 120  
 AAATAAAGCA GTATGCGAGC GCTTGACTAA AAAAAATTGT ACATTGAAAA CTAGATAAGT 180  
 30 AAGTAAAATA TAGATTTTAC CAAGCAAAAC CGAGTGAATA AAGAGTTTAA AATAAGCTTG 240  
 AATTCATAAG AAATAATCGC TAGTGTTTGA AAGAACACTC ACAAGATTAA TAACGCGTTT 300  
 AAATCTTTTT ATAAAAGAAC GTAACCTTCAT GTTAACGTTT GACTTATAAA AATGGTGGAA 360  
 35 ACATA 365

## (2) INFORMATION FOR SEQ ID NO: 140:

40 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 548 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 140:

CTAAGGATAT ATTCGGAACA TCTTCTTCAG AAGATGCGGA ATAACGTGAC ATATTGTATT 60  
 55 CAGTTTTGAA TGTTTATTTA ACATTCAAAT ATTTTTTGGT TAAAGTGATA TTGCTTATGC 120

GAGCNCTTGA CAATCTATTC TTTTAAAGA AAGCGTTGT CAGACAATGC ATTAAGAAAA 180  
 ATTAAAGCGG AGTTTACTTT TGTAATGAG CATTGATTT TTTGAAAATA AAGCAGTATG 240  
 5 CGAGCGCTTG ACTAAAAGA AATTGTACAT TGAAACTAG ATAAGTAAGT AAAATATAGA 300  
 TTTTACCAAG CAAAACCGAG TGAATAAGA GTTTTAAATA AGCTTGAATT CATAAGAAAT 360  
 10 AATCGCTAGT GTTCGAAAGA AACTCACAA GATTAATAAC GCGTTTAAAT CTTTTATAA 420  
 AAGAAACGT TTAGCAGACA ATGAGTTAAA TTATTTTAAA GCAGAGTTTA CTTATGTAAA 480  
 TGAGCATTTA AAATAATGAA AACGAAGCCG TATGTAGCA TTTGACTTAT AAAAATGGTG 540  
 15 GAAACATA 548

## (2) INFORMATION FOR SEQ ID NO: 141:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 471 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 141:

CTAAGGATAT ATTCGGAACA TCTTCTCAG AAGATCGGA ATAACGTGAC ATATTGTATT 60  
 CAGTTTTGAA TGTTTATTTA ACATTCAAAT ATTTTTTGGT TAAAGTGATA TTGCTTATGC 120  
 35 GAGCGCTTGA CAATCTATTC TTTTAAAGA AAGCGTTGT CAGACAATGC ATTAAGAAAA 180  
 ATTAAAGCGG AGTTTACTTT TGTAATGAG CATTGATTT TTTGAAAATA AAGCAGTATG 240  
 40 CGAGCGCTTG ACTAAAAGA AATTGTACAT TGAAACTAG ATAAGTAAGT AAAATATAGA 300  
 TTTTACCAAG CAAAACCGAG TGAATAAGA GTTTTGAATA AGCTTGAATT CATAAGAAAT 360  
 AATCGCTAGT GTTCGAAAGA AACTCACAA GATTAATAAC GCGTTTAAAT CTTTTATAA 420  
 45 AAGAACGTAA CTTCATGTTA ACGTTTGA CTATAAAATG GTGGAAACAT A 471

## (2) INFORMATION FOR SEQ ID NO: 142:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 383 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 142:

CTAAGGATAT ATTCGGAACA TCTTCTTCAG AAGATGCGGA ATAACGTGAC ATATTGTATT 60  
 10 CAGNTTTGAA TGTTTATTTA ACATTCAAAA AATGGGCCTA TAGCTCAGCT GGTAGAGCG 120  
 CACGCCTGAT AAGCGTGAGG TCGGTGGTTC GAGTCCACTT AGGCCACCA TTATTTGTAC 180  
 ATTGAAAAC AGATAAGTAA GTAAATATA GATTTTACCA AGCAAACCG AGTGAATAAA 240  
 15 GAGTTTAAA TAAGCTTGAA TTCATAAGAA ATAATCGCTA GTGTCGAAA GAACACTCAC 300  
 AAGATTAATA ACGCGTTTAA ATCTTTTAT AAAAGAACGT AACTTCATGT TAACGTTTGA 360  
 CTTATAAAAA TGGTGGAAC ATA 383

20

(2) INFORMATION FOR SEQ ID NO: 143:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 351 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

25

(ii) MOLECULE TYPE: cDNA

30

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 143:

CTAAGGATAT ATTCGGAACA TCTTCYTCAG AAGATGCGGA ATAATGTGAC ATATTGTATT 60  
 CAGTTTGTAA TGTTTATTTA ACATTCAAAT ATTTTGGT TAAAGTGATA TTGCTTATGC 120  
 40 GAGCGCTGA CTA AAAAGAA ATTGTACATT GAAACTAGA TAAGTAAGTA AAANTATAGA 180  
 TTTTACCAAG CAAAACCGAG TGAATAAAGA GTTTTAAATA AGCTTGAATT CATAAGAAAT 240  
 AATCGCTAGT GTTCGAAAGA AACTCACAA GATTAATAAC GCGTTTAAAT CTTTATATA 300  
 45 AAGAACGTAA CTTCATGTTA ACGTTTGACT TATAAAATG GTGGAACAT A 351

45

(2) INFORMATION FOR SEQ ID NO: 144:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 263 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: cDNA

55

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 144:

10	CTAAGGATAT ATTCGGAACA TCTTCTACGA AGATGAGGGA ATAACGTGAC ATATTGTATT	60
	CAGTTTTGAA TGTTTATTAA CATTCAATTG TACATTGAAA ACTAGATAAG TAAGTAAGAT	120
	TTTACCAAGC AAAACCGAGT GAATAGAGTT TTAAATAAGC TTGAATTCAT AAATAATCGC	180
15	TAGTGTTCGA AAGACNTCCA CAAGATTAAT AACTAGTTTT AGCTATTTAT TTTGAATAAC	240
	AATTCAAAAT ATGGTGGGAC ATA	263

(2) INFORMATION FOR SEQ ID NO: 145:

20 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 247 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

25

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 145:

35	AAGGATAAGG AACTGCACAT TGGTCTTGTT TAGTCTTGAG AGGTCTTGTT GGGCCTTAGC	60
	TCAGCTGGGA GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTTCGATCC CGCTAGGCTC	120
	CATTGGTGAG AGATCACCAA GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA	180
40	ACAAGAAAAT AAACCGAAAA CGCTGTAGTA TTAATAAAGA GTTTATGACT GAAAGGTCAA	240
	AAAATAA	247

(2) INFORMATION FOR SEQ ID NO: 146:

45 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 375 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 146:

5	AAGGAAATGG AACACGTTTA TCGTCTTATT TAGTTTGTAG AGGTCTTGTG GGGCCTTAGC	60
	TCAGCTGGGA GAGCGCCTGC TTNGCACGCA GGAGGTCAGC GGTTCGATCC CGCTAGGCTC	120
	CATCAGGATA CANTCCTACT AAACCTTAATA CAAGTGAAGT TGAACACGCA ACTCACTTCC	180
10	TAGGAAAATA GACAATCTTC GCTTGTGTGC AAGGCACACA TGGTCAGATT CCTAATTTTC	240
	TACAGAAGTT TCGCTAAAGC GAGCGTTGCT TAGTATCCTA TATAATAGTC CATNGAAAAT	300
	TGAATATCTA TATCAAATTC CACGATCTAG AAATAGATTG TGGAAACGTA ACAAGAAATT	360
15	AACCCGNAAA CGCTG	375

(2) INFORMATION FOR SEQ ID NO: 147:

	(i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 244 base pairs
	(B) TYPE: nucleic acid
	(C) STRANDEDNESS: single
	(D) TOPOLOGY: linear

25	(ii) MOLECULE TYPE: cDNA
----	--------------------------

	(iii) HYPOTHETICAL: NO
--	------------------------

	(iii) ANTI-SENSE: NO
--	----------------------

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 147:

	AAGGATAAGG AACTGCACAT TGGTCTTGTT TAGTCTTGAG AGGTCTTGTG GGGCCTTAGC	60
35	TCAGCTGGGA GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTTCGATCC CGCTAGGCTC	120
	CATTGGTGAG AGATCACCAA GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA	180
	ACAAGAAAAT AAACCGAAAC GCTGTAGTAT TAAAAGAGTT TATGACTGAA AGGTCAGAAA	240
40	ATAA	244

(2) INFORMATION FOR SEQ ID NO: 148:

	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 284 base pairs
	(B) TYPE: nucleic acid
	(C) STRANDEDNESS: single
	(D) TOPOLOGY: linear

50	(ii) MOLECULE TYPE: cDNA
----	--------------------------

	(iii) HYPOTHETICAL: NO
--	------------------------

	(iii) ANTI-SENSE: NO
--	----------------------

55



## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 148:

5 CTAAGGATAT ATTCGGAACA TCTTCTTACG AAGATGCAGG AATAACATTG ACATATTGTA 60  
 TTCAGNTGTG AATGCTCATT GGAGNATTCA TNGCATNATT TGGTNCATTG ACANCTAGAT 120  
 AAGNAAGTAA AATTTATGAT TTTACCAAGC AAAACCGAGT GAATTAGAGT TNTNNAACAA 180  
 10 GCTTTGATT CAAAAAGAAA TAATCGCTAG TGTTGAAAG AACACTCACA GATTANTAAC 240  
 ATCTTGGGTT TTCACCCGAC TTGTTCTGTT CGAAAGTCAA AAAA 284

## (2) INFORMATION FOR SEQ ID NO: 149:

15 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 246 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

25

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 149:

AAGGATAAGG AACTGCGCAT TGGTCTTGTT TAGTCTTGAG AGGTCTTGTT GGGCCTTAGC 60  
 30 TCAGCTGGGA GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTTCGATCC CGCTAGGCTC 120  
 CATTGGTGAG AGATCACCAA GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA 180  
 35 ACAAGAAAAT AAACCGAAAA CGCTGTAGTA TTAATAAGAG TTTATGACTG AAAGGTCAAA 240  
 AAATAA 246

## (2) INFORMATION FOR SEQ ID NO: 150:

40 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 247 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

50

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 150:

AAGGATAAGG AACTGCGCAT TGGTCTTGTT TAGTCTTGAG AGGTCTTGTT GGGCCTTAGC 60  
 55 TCAGCTGGGA GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTTCGATCC CGCTAGGCTC 120

CATTGGTGAG AGATCACCAA GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA 180  
 5 ACAAGAAAAT AAACCGAAAA CGCTGTAGTA TTAATAAGAG TTTATGACTG AAAGGTCAGA 240  
 AAAATAA 247

(2) INFORMATION FOR SEQ ID NO: 151:

10 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 247 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

20 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 151:

25 AAGGAAAAGG AACTGCGCAT TGGTCTTGTT TAGTCTTGAG AGGTCTTGTT GGGCCTTAGC 60  
 TCAGCTGGGA GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTTCGATCC CGCTAGGCTC 120  
 CATTGGTGAG AGATCACCAA GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA 180  
 30 ACAAGAAAAT AAACCGAAAA CGCTGTAGTA TTAATAAGAG TTTATGACTG AAAGGTCAGA 240  
 AAAATAA 247

(2) INFORMATION FOR SEQ ID NO: 152:

35 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 244 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

45 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 152:

50 AAGGATAAGG AACTGCGCAT TGGTCTTGTT TAGTCTTGAG AGGTCTTGTT GGGCCTTAGC 60  
 TCAGCTGGGA GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTTCGATCC CGCTAGGCTC 120  
 CATTGGTGAG AGATCACCAA GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA 180  
 55 ACAAGAAAAT AAACCGAAAC GCTGTAGTAT TAAAGAGTT TATGACTGAA AGGTCAGAAA 240

ATAA

244

## (2) INFORMATION FOR SEQ ID NO: 153:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 243 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 153:

AAGGATAAGG AACTGCGCAT TGGTCTTGTT TAGTCTTGAG AGGTCTTG TG GGGCCTTAGC	60
TCAGCTGGGA GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTTCGATCC CGCTAGGCTC	120
CATTGGTGAG AGATCACCAA GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA	180
ACAAGAAAAT AAACCGAAAC GCTGTAGTAT TAAAAGAGTT TATGACTGAA AGGTCAAAAA	240
TAA	243

## (2) INFORMATION FOR SEQ ID NO: 154:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 809 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 154:

TAAGGAAGAT CGAGAATTGG AAAGAGGTCG GATTTATCCG GATGATCCTT CTCCATCTTA	60
TTAGAACATA GATCGCAGGC CAGTCAGCCT GACGATCGCT TGCAGGCGTG CCGCCTTCGT	120
TTCTCTTTCT TCATTGTTGA TTGCTCACGG GCCGTACCGC AGCTGACGCT GCTGGCCCTG	180
CGCAGGCGCG GCCCATCAGG GCCGAACGGC CGGTCGGCCT TGCNAAGCTT CGCTTCGGGG	240
TGGATCTGTG GATCGCGTAG TAGCGTTTGC GTCGGTATCT GGGCTTGTAG CTCAGTTGGT	300
TAGAGCACAC GCTTGATAAG CGTGGGGTCG GAGGTTCAAG TCCTCCCAGG CCCACCAAGT	360
TACTTGATGA GGGGCCGTAG CTCAGCTGGG AGAGCACCTG CTTTGCAAGC AGGGGGTCGT	420

CGGTTTCGATC CCGTCCGGCT CCACCATCAT GTTGGTGTG AGACGGATAT TGGCAATCAA 480  
5 CAAAAGAAAG AAACAAGTTT GCGGACTNTT ACGAAAGTCT GCCTGTTCTG TATGAAATCG 540  
TGAAGAGAAG ATGTAATCGG ATCAACTGAA GAGTTGATGT CGCAAGAAGC TTGCTCAAGC 600  
CTTGCAATAT GATTGATGTG TTTAACCGCC ATCACCGATT GTATCTCGAG AAGCTGGTCT 660  
10 TTCTGCTGAT ACTGTTGAAA CGAGCATTTG CAGTCGAATG GCAACATTCT GCGTCGCATA 720  
ATGCGGCTTT AAGAGCTGAG TTTTGATGGA TATTGGCAAT GAGAGTGATC AAGTGTCTTA 780  
AGGGCATTGG TGGATGCCTT GGCATGCAC 809  
15 (2) INFORMATION FOR SEQ ID NO: 155:  
(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 23 base pairs  
(B) TYPE: nucleic acid  
20 (C) STRANDEDNESS: single  
(D) TOPOLOGY: linear  
(ii) MOLECULE TYPE: cDNA  
(iii) HYPOTHETICAL: NO  
25 (iii) ANTI-SENSE: NO  
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 155:  
30 TGGGGTGAAG TCGTAACAAG GTA 23  
(2) INFORMATION FOR SEQ ID NO: 156:  
35 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear  
40 (ii) MOLECULE TYPE: cDNA  
(iii) HYPOTHETICAL: NO  
(iii) ANTI-SENSE: NO  
45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 156:  
50 CCTTCCCTC ACGGTACTGG T 21  
(2) INFORMATION FOR SEQ ID NO: 157:  
(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 277 base pairs  
55 (B) TYPE: nucleic acid  
(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 157:

AAGGAGCACC	ACGAGAAACA	CTCCAATTGG	TGGGGTGTAA	GCCGTGAGGG	GTTCTCGTCT	60
GTAGTGGACG	GAAGCCGGGT	GCACAACAAC	AAGCAAGCCA	GACACACTAT	TGGGTCCTGA	120
GGCAACATCT	CTGTTGGTTT	CGGGATGTTG	TCCCACCATC	TTGGTGGTGG	GGTGTGGTGT	180
TTGAGAATTG	GATAGTGGTT	GCGAGCATCA	ATTGGATGCG	CTGCCTTTTG	GTGGCGTGTT	240
CTGTTGTGCA	ATTTTATTCT	TTGGTTTTTG	TGTTTAT			277

(2) INFORMATION FOR SEQ ID NO: 158:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 286 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 158:

AAGGAGCACC	ACGAGAAACA	CCCCAATTGG	TGGGGTGTGA	GCCGTGAGGG	GTTCTCGTCT	60
GTAGTGGACG	AGGGCCGGGT	GCACAACAAC	AGGCAATCGC	CGGACACACT	ATTGGGCCCT	120
GAGACAACAC	TCGGCCGACT	GAGGTCGACG	TGGTGTCCCT	CCATCTTGGT	GGTGGGGTGT	180
GGTGTTTGAG	CATTGAATAG	TGGTTGCGAG	CATCTAGCCG	GATGCGTTCC	CCAGTGGTGC	240
CGGTTGCTCA	AAAATGTGTA	ATTTTCTTT	TGGTTTTTGT	GTTTCGT		286

(2) INFORMATION FOR SEQ ID NO: 159:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 286 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 159:

10	AAGGAGCACC ACGAGAAACA CCCCAATTGG TGGGGTGTGA GCCGTGAGGG GTTCTCGTCT	60
	GTAGTGGACG AGGGCCGGGT GCACAACAAC AGGCAATCGC CGGACACACT ATTGGGCCCT	120
	GAGACAACAC TCGGCCGACT GAGGTCGACG TGGTGTCCCT CCATCTTGGT GGTGGGGTGT	180
15	GGTGTTTGAG CATTGAATAG TGGTTGCGAG CATCTAGACG GATGCGTTCC CCAGTGGTGC	240
	GCGTTCGTCA AAAATGTGTA ATTTTCTTT TGGTTTTTGT GTTCGT	286

(2) INFORMATION FOR SEQ ID NO: 160:

20

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 279 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

25

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 160:

35	AAGGAGCACC ACGAGAAACA CCCCAATTGG TGGGGTGTGA GCCGTGAGGG GTTCTCGTCT	60
	GTAGTGGACG AGGCGGGTAC AACAAACGCCA ATCGCCGGAC AACTATTGG GCCTGAGACA	120
	AACTCGGCC GACTGAGGTC GACGTGGTGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT	180
40	TGAGCATTGA ATAGTGGTTG CGAGCATCTA GCCGGATGCG TTCCCCAGTG GTGCGCGTTC	240
	GTCAAAAATG TGTAATTTT CTTTGGTTTT TGTGTTCGT	279

(2) INFORMATION FOR SEQ ID NO: 161:

45

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 288 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 161:

5 AAGGAGCACC ACGAGAAACA CTCCAATTGG TGGAGTGTGA GCCGTGAGGG GTTCTCGTCT 60  
 GTAGTGGACG AGGGCCGGGT GCACAACAGC AGACAATCGC CAGACACACT ATTGGGCCCT 120  
 GAGACAACAC TCGGCCGACT TTGGTCGACG TGGTGTCCCT CCATCTTGGT GGTGGGGTGT 180  
 10 GGTGTTTGAG CATTGAATAG TGGTTGCGAG CATCTAGACG GATGCGTTGC CCTCGGGCCG 240  
 CGTGTTTCGTC AAAAATGTGT AATTTTTTCT TTTGGTTTTT GTGTTCGT 288

## (2) INFORMATION FOR SEQ ID NO: 162:

15 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 289 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

25 (iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 162:

30 AAGGAGCACC ACGAGAAACA CTCCAATTGG TGGAGTGTGA GCCGTGAGGG GTTCTCGTCT 60  
 GTAGTGGACG GGAGCCGGGT GCACAACAAC AGGCAATCGC CAGACACACT ATTGGGCCCT 120  
 GAGACAACAC TCGGCCGGCT TTGAGTCGAA GTGGTGTCCC TCCATCTTGG TGGTGGGGTG 180  
 35 TGGTGTTTGA GCATTGAATA GTGGTTGCGA GCATCTAGAC GGATGCGTTG CCTTCGGGCC 240  
 GCGTGTTTCGT CAAAAATGTG TAATTTTTTC TTTGGTTTTT TGTGTTCGT 289

## (2) INFORMATION FOR SEQ ID NO: 163:

40 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 232 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

50 (iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 163:

55 AGGGAGCACC GAAACGCATC CCGCGTGGGG TGTTGGTTTC CCGTCTTCTC GCGTCGGCCG 60

AGGTGTTGGG CAGCAGGCAG TAACCCCGGA AACTGTGTGG GTTTTGAGAA CACCCGTGGT 120  
 GGTGTTGTGC TCCCGTGGT GCGGGGTGTG GTGTTTGAGT GTTGATAGT GGTGCGAGC 180  
 5 ATCTGGCAAA GACTGTGGTA AGCGGTTTTT GTTGATGTTT TCTGGTGTTT GT 232

## (2) INFORMATION FOR SEQ ID NO: 164:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 279 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: cDNA

## (iii) HYPOTHETICAL: NO

## (iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 164:

AAGGAGCACC ACGAGAAACA CTCCAATTGG TGGGGTGTGA GCCGTGAGGG GTTCTCGTCT 60  
 25 GTAGTGGACG AGGGCGGGTG CACAACAACA GCAATCGCCA GACACACTAT TGGCCCTGAG 120  
 ACAACACTCG GCCGACTTGG TTGAAGTGGT GTCCCTCCAT CTGGTGGTG GGGTGTGGTG 180  
 TTTGAGTATT GGATAGTGGT TGCAGCATC TAATGAACGC GTCGCCGCAA CGGTTACGTG 240  
 30 TTCGTTTTGT GTAATTTTTC TATTGGTTTT TGTGTTCTGT 279

## (2) INFORMATION FOR SEQ ID NO: 165:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 285 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: cDNA

## (iii) HYPOTHETICAL: NO

## (iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 165:

AAGGAGCACC ACGAGAAACA CTCCAATTGG TGGGGTGTGA GCCGTGAGGG GTTCTCGTCT 60  
 50 GTAGTGGACG AGGGCCGGGT GCACAACAAC AGGCAATCGC CAGACACACT ATTGGCCCTG 120  
 AGACAACACT CGGCCGACTT TGGTCGAAGT GGTGTCCCCC CATCTTGGTG GTGGGGTGTG 180  
 GTGTTTGAGT ATTGGATAGT GGTGCGAAC ATCTAAATGA ACGCGTTGCC GGCAACGGTT 240  
 55 ACGTGTTCTG TTAGTGTAA TTTTCTAAT GGTTTTGTG TTCGT 285



## (2) INFORMATION FOR SEQ ID NO: 166:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 384 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: cDNA

## (iii) HYPOTHETICAL: NO

## (iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 166:

AAGGAGCACC ACGAGACCTG GGCCGGCCCC GCAGATCGCG GGATCAGCTG AGCTTTCAGG	60
CGATTCGTTG GATGGCCTCG CACCTGTAGT GGGTGGGGGT CTGGTGCACT CAACAAACTT	120
GGCGTGGGAT GCGGGAAAGC ATCTGCGGAA AATCATCAGA CACACTATTG GGCTTTGAGA	180
CAACAGGCCC GCAGCCTGCC CGTTGGGGGC AGGGGTGTGT TGTTCCTCA CTTTGGTGGT	240
GGGGGTGGTG TTTGATTGTG GGATAGTGGT TGCAGCATC TAGCGCGCAG AATGTGTGGT	300
CTCACTCCTT GTGGGTGGGG CCTGGTTTTG TGTGCGATTG ATGTGCAATT TCTTTGAAA	360
CTCATTTTTT GGTTTTTGTG TTGT	384

## (2) INFORMATION FOR SEQ ID NO: 167:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 295 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: cDNA

## (iii) HYPOTHETICAL: NO

## (iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 167:

AAGGAGCACC ACGAAAACT CCCCAATTGG TGGGGTGTA GCGTGAGGG GTTCCCGTCT	60
GTAGTGGACG GGGGCCGGGT GCGCAACAGC AAGCGAAACG CCGGACACAC TATTGGGTCC	120
TGAGGCAACA CTCGGGTTTG TCCCCCTCAG GGATTTCTG GGTGTTGTCC CACCATCTTG	180
GTGGTGGGGT GTGGTGTTTG AGAATTGGAT AGTGGTTGCG AGCATCAAAT GGATGCGTTG	240
CCCCTACGGG TAGCGTGTC TTTTGTGCAA TTTTATTCTT GGTTTTTGTG TTTGT	295

## (2) INFORMATION FOR SEQ ID NO: 168:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 279 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 168:

AAGGAGCACC	ACGAGAAGCA	CTCCAAGTGG	TGGGGTGCAA	GCCGTGAGGG	GTTCTCGTCT	60
GTAGTGGACG	AGAGCCGGGT	GCGCGACAAC	GAACGAGCCA	GACACACTAT	TGGGTCCTGA	120
GGCAACACTC	GGGCTTGGCC	AGAGCTGTTG	TCCCACCATC	TTGGTGGTGG	GGTGTGGTGT	180
TTGAGAATTG	GATAGTGGTT	GCGAGCATCA	AATGGATGCG	TTGCCCCCTAC	GGGTGGCGTG	240
TTCTTTTGTG	CAATTTTATT	CTTTGGTTTT	TGTGTTTGT			279

## (2) INFORMATION FOR SEQ ID NO: 169:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 286 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 169:

AAGGAGCACC	ACGAAAAACA	CCCCAAGTGG	TGGGGTGTA	GCCGTGAGGG	GCTCCCGTCT	60
GTAGTAGACG	GGCGCCGGGT	GCGCAACAGC	AAGCGAGCCA	GACACACTAT	TGGGTCCTGA	120
GGCAACACTC	GGGCTTGTCT	TGGACTCGTC	CAAGAGTGTT	GTCCCACCAT	CTTGGTGGTG	180
GGGTGTGGTG	TTTGAGAATT	GGATAGTGGT	TGCGAGCATC	ACTGGATGCG	TTGCCCCCAG	240
GGGTAGCGTG	TTCTTTTGTG	CAATTATTC	TGGTTTGTGT	GTTAGT		286

## (2) INFORMATION FOR SEQ ID NO: 170:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 265 base pairs
  - (B) TYPE: nucleic acid

(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 170:

AAGGAGCACC ACGAAAAACA CTCCGCATCC GGTGGGGTGT GAGCCGTGAG GGAGCCCGTG	60
15 CCTGTAGTGG GTGTGGGTTG GGTGCGCGAC AACAAATGGG AAAAATCGCT GGGCACACTA	120
TTGGGCTTTG AGGCAACACC TGGTTTGTTT TGGGTGGTGT CGCTCCATCT TGGTGGTGGG	180
GTGTGGTGTG TGAGTTGTGG ATAGTGGTTG CGAGCATCTA AGCAAAAGCT GTTGTGTTGAC	240
20 GGTTTTTGTC GAGTGTGTG TGTGT	265

(2) INFORMATION FOR SEQ ID NO: 171:

25 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 299 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 171:

AAGGAGCACC ACGAAAAACA CTCCAATTGG TGGGGTGTA GCGGTGAGGG GTTCTCATCT	60
40 GTAGTGGACG AGAGCCGGGT GCACAACAGC AAATGAATCG CCAGACACAC TGTGGGTCC	120
TGAGGCAACA CTCAGGCTTG TCCCATGTTG GGCTTGATCG GGTGCTGTCC CCCCATCTTG	180
GTGGTGGGGT GTGGTGTGTT AGTATGGAT AGTGGTTGCG AGCATCTAAA TGGATACGTT	240
45 GCCAGTAATG GTGGCGTATT CATTGAAAAT GTGTAATTTT CTTCTTTGGT TTTGTGTGT	299

(2) INFORMATION FOR SEQ ID NO: 172:

50 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 299 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

55 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 172:

10	AAGGAGCACC ACGAAAAACA CTCCAATTGG TGGGGTGTA	60
	AGCCGAGGG GTTCTCATCT	
	GTAGTGGACG AGAGCCGGGT GCACAACAGC AAATGAATCG	120
	CCAGACACAC TGTGGGTCC	
	TGAGGCAACA CTCAGGCTTG TCCCATGTTG GGCTTGATCG	180
	GGTGCTGTCC CCCCATCTTG	
15	GTGGTGGGGT GTGGTGTGTTG AGTATTGGAT AGTGGTTGCG	240
	AGCATCTAAA TGGATACGTT	
	GCCAGTAATG GTGGCGTGTT CATTGAAAAT GTGTAATTTT	299
	CTTCTTTGGT TTTGTGTGT	

(2) INFORMATION FOR SEQ ID NO: 173:

20 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 298 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

25

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 173:

35	AAGGAGCACC ACGAAAAACA CTCCAATTGG TGGGGTGTA	60
	AGCCGAGGG GTTCTCATCT	
	GTAGTGGACG AGAGCCGGGT GCACAACAGC AAATGAATCG	120
	CCAGACACAC TGTGGGTCC	
	TGAGGCAACA CTCAGGCTTG TCCCATGTTG GGCTTGATCG	180
	GGTGCTGTCC CCCCATCTTG	
40	GTGGTGGGGT GTGGTGTGTTG AGTATTGGAT AGTGGTTGCG	240
	AGCATCTAAA TGGAACGTTG	
	CCAGTAATGG TGGCGTGTTT ATTGAAAATG TGTAATTTTC	298
	TTCTTTGGTT TTGTGTGT	

(2) INFORMATION FOR SEQ ID NO: 174:

45 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 300 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 174:

5	AAGGAGCACC ATTTCTCAGT CGAATGAACT GAGAACATAA AGCGAGTATC TGTAGTGGAT	60
	ACATGCTTGG TGAATATGTT TTATAAATCC TGTCCACCCC GTGGATAGGT AGTCGGCAAA	120
	ACGTCGGACT GTCATAAGAA TTGAAACGCT GGCACACTGT TGGGTCCTGA GGCAACACAT	180
10	TGTGTTGTCA CCCTGCTTGG TGGTGGGGTG TGGTCCTTGA CTTATGGATA GTGGTTGCGA	240
	GCATCTAAAC ATAGCCTCGC TCGTTTTTCGA GTGAGGCTGG TTTTGGCAAT TTTATTAGCT	300

(2) INFORMATION FOR SEQ ID NO: 175:

15	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 22 base pairs
	(B) TYPE: nucleic acid
	(C) STRANDEDNESS: single
	(D) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: cDNA
	(iii) HYPOTHETICAL: NO
25	(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 175:

30	GGTTTCGGGA TGTTGTCCCA CC	22
----	--------------------------	----

(2) INFORMATION FOR SEQ ID NO: 176:

35	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 21 base pairs
	(B) TYPE: nucleic acid
	(C) STRANDEDNESS: single
	(D) TOPOLOGY: linear
40	(ii) MOLECULE TYPE: cDNA
	(iii) HYPOTHETICAL: NO
45	(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 176:

50	CGACTGAGGT CGACGTGGTG T	21
----	-------------------------	----

(2) INFORMATION FOR SEQ ID NO: 177:

55	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 27 base pairs
	(B) TYPE: nucleic acid
	(C) STRANDEDNESS: single
	(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

5 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 177:

GGTGTGTTGAG CATTGAATAG TGGTTGC 27

(2) INFORMATION FOR SEQ ID NO: 178:

15 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 178:

30 GTTGGGCAGC AGGCAGTAAC C 21

(2) INFORMATION FOR SEQ ID NO: 179:

35 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 20 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 179:

CCGGCAACGG TTACGTGTTT 20

(2) INFORMATION FOR SEQ ID NO: 180:

50 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

55 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 180:

TCGTGGATG GCCTCGCACC T

(2) INFORMATION FOR SEQ ID NO: 181:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 181:

ACTTGCGTG GGATGCGGGA A

(2) INFORMATION FOR SEQ ID NO: 182:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 24 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 182:

CCCTCAGGGA TTTTCTGGGT GTTG

(2) INFORMATION FOR SEQ ID NO: 183:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 183:

GGACTCGTCC AAGAGTGTG TCC

(2) INFORMATION FOR SEQ ID NO: 184:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 21 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 184:

TCGGGCTTGG CCAGAGCTGT T

(2) INFORMATION FOR SEQ ID NO: 185:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 20 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 185:

GGGTGCGCAA CAGCAAGCGA

(2) INFORMATION FOR SEQ ID NO: 186:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 19 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA



(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 186:

GATGCGTTGC CCCTACGGG

19

10

(2) INFORMATION FOR SEQ ID NO: 187:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 24 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

15

(ii) MOLECULE TYPE: cDNA

20

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 187:

CCCTACGGGT AGCGTGTCT TTTG

24

30

(2) INFORMATION FOR SEQ ID NO: 188:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 23 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

35

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

40

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 188:

45

CGGATCGATT GAGTGCTTGT CCC

23

(2) INFORMATION FOR SEQ ID NO: 189:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 23 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: cDNA

55

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 189:

TCTAAATGAA CGCACTGCCG ATG

23

10

(2) INFORMATION FOR SEQ ID NO: 190:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 20 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

15

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

20

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 190:

25

TGAGGGAGCC CGTGCCTGTA

20

(2) INFORMATION FOR SEQ ID NO: 191:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 22 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 191:

CATGTTGGGC TTGATCGGGT GC

45

22

(2) INFORMATION FOR SEQ ID NO: 192:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 20 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

55

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 192:

CCTGGGTTTG ACATGCACAG

20

10

(2) INFORMATION FOR SEQ ID NO: 193:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

15

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

20

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 193:

25

GCGTAGTAGC GTTGCGTCG G

21

(2) INFORMATION FOR SEQ ID NO: 194:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: cDNA

35

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 194:

CGCAAGAAGC TTGCTCAAGC C

21

45

(2) INFORMATION FOR SEQ ID NO: 195:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 470 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

55

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 195:

CCTAATGATA TTGATTCGCG TGAAGTGCTC ACACAGATTG TCTGATGAAA AAGTAACGAG 60  
 CAGAAATACC TTTATAGGCT TGTAGCTCAG GTGGTTAGAG CGCACCCCTG ATAAGGGTGA 120  
 GGTCCGGTGGT TCAAGTCCAC TCAGGCCTAC CACTTCTCGA AGTGGAAAAG GTACTGCACG 180  
 TGACTGTATG GGGCTATAGC TCAGCTGGGA GAGCGCCTGC CTTGCACGCA GGAGGTCAGC 240  
 GGTTGATCC CGCTTAGCTC CACCATATAG TCCTGTATTT CAATACTTCA GAGTGTACTG 300  
 GCAACAGTAT GCTGCCAAGT ATTTTGCTCT TTAACAATCT GGAACAAGCT GAAAATTGAA 360  
 ACATGACAGC TGAAACTTAT CCCTCCGTAG AAGTATTGGG GTAAGGATTA ACCTGTCATA 420  
 GAGTCTCTCA AATGTAGCAG CACGAAAGTG GAAACACCTT CGGGTTGTGA 470

(2) INFORMATION FOR SEQ ID NO: 196:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 453 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 196:

CCTAATGATA TTGATTCGCG TGAAGTGCTC ACACAGATTG TTTGATAGAA ACGTAATGAG 60  
 CAAAAGCGCT ACCTGTTGAT GTAATGAGTC ACTGACTCAT GCTGATACGA ACCGATTAAG 120  
 ACAGTCAGTT TAATCGGATT TTCGTGTCCC CATCGTCTAG AGGCCTAGGA CACTGCCCTT 180  
 TCACGGCTGT AACAGGGGTT CGAATCCCCT TGGGGACGCC ATTCGATAAT GAGTGAAAGA 240  
 CATTATCACC GGTCTTGGA ACCGAAAACA TCTTAAAGAT GACTCTTGCG AGTCGTGTTT 300  
 AAGATATTGC TCTTTAACA TCTGGAACAA GCTGAAAATT GAAACATGAC AGCTGAAACT 360  
 TATCCCTCCG TAGAAGTATT GGGGTAAGGA TTAACCTGTC ATAGAGTCTC TCAAATGTAG 420  
 CAGCACGAAA GTGGAAACAC CTTCGGGTTG TGA 453

(2) INFORMATION FOR SEQ ID NO: 197:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 248 base pairs  
 (B) TYPE: nucleic acid

(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA  
(iii) HYPOTHETICAL: NO  
(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 197:

TAAGGATAAG GAAGAAGCCT GAGAAGGTTT CTGACTAGGT TGGGCAAGCA TTTATATGTA	60
AGAGCAAGCA TTCTATTTCA TTTGTGTTGT TAAGAGTAGC GCGGTCAGGA CGAGACATAT	120
AGTTTGTGAT CAAGTATGTT ATTGTAAAGA AATAATCATG GTAACAAGTA TATTTACGCG	180
ATAATAATAG ACGTTTAAAGA GTATTGTCT TTTAGGTGAA GTGCTTGCAAT GGATCTATAG	240
AAATTACA	248

(2) INFORMATION FOR SEQ ID NO: 198:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 23 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA  
(iii) HYPOTHETICAL: NO  
(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 198:

GGAAAAGGTA CTGCACGTGA CTG	23
---------------------------	----

(2) INFORMATION FOR SEQ ID NO: 199:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 23 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA  
(iii) HYPOTHETICAL: NO  
(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 199:

GACAGCTGAA ACTTATCCCT CCG

23

(2) INFORMATION FOR SEQ ID NO: 200:

- (i) SEQUENCE CHARACTERISTICS:  
    (A) LENGTH: 25 base pairs  
    (B) TYPE: nucleic acid  
    (C) STRANDEDNESS: single  
    (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 200:

GCTACCTGTT GATGTAATGA GTCAC

25

(2) INFORMATION FOR SEQ ID NO: 201:

- (i) SEQUENCE CHARACTERISTICS:  
    (A) LENGTH: 22 base pairs  
    (B) TYPE: nucleic acid  
    (C) STRANDEDNESS: single  
    (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 201:

GAGTAGCGCG GTGAGGACGA GA

22

(2) INFORMATION FOR SEQ ID NO: 202:

- (i) SEQUENCE CHARACTERISTICS:  
    (A) LENGTH: 25 base pairs  
    (B) TYPE: nucleic acid  
    (C) STRANDEDNESS: single  
    (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 202:

CTTTTATGTC AGATAAAGTA TGCAA

25

(2) INFORMATION FOR SEQ ID NO: 203:

- (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

5

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

10

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 203:

15

CGTAAAAGGG TATGATTATT TG

22

(2) INFORMATION FOR SEQ ID NO: 204:

(i) SEQUENCE CHARACTERISTICS:

20

(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

25

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 204:

TCGAGAATTG GAAAGAGGTC

20

35

(2) INFORMATION FOR SEQ ID NO: 205:

(i) SEQUENCE CHARACTERISTICS:

40

(A) LENGTH: 19 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

45

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 205:

50

AAGAGGTCGG ATTTATCCG

19

(2) INFORMATION FOR SEQ ID NO: 206:

(i) SEQUENCE CHARACTERISTICS:

55

(A) LENGTH: 18 base pairs

(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

5

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

10

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 206:

15

TTCGACTGCA AATGCTCG

18

(2) INFORMATION FOR SEQ ID NO: 207:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 19 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

20

(ii) MOLECULE TYPE: cDNA

25

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 207:

TCTTAAAGCC GCATTATGC

19

(2) INFORMATION FOR SEQ ID NO: 208:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

35

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

45

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 208:

50

CCTAATGATA TTGATTCGCG

20

(2) INFORMATION FOR SEQ ID NO: 209:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid

55



(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA  
(iii) HYPOTHETICAL: NO  
(iii) ANTI-SENSE: NO

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 209:

ATGACAGGTT AATCCTTACC CC

22

15

(2) INFORMATION FOR SEQ ID NO: 210:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 25 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

20

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

25

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 210:

30

GGTGTGGTCC TTGACTTATG GATAG

25

(2) INFORMATION FOR SEQ ID NO: 211:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

35

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

40

(iii) ANTI-SENSE: NO

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 211:

TCGGGCCGCG TGTTTCGTCAA A

21

50

(2) INFORMATION FOR SEQ ID NO: 212:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 24 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single

55

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 212:

CGTTTTTCATA AGCGATCGCA CGTT

24

(2) INFORMATION FOR SEQ ID NO: 213:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 235 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 213:

TAAGGATAAG GAAACCTGTG AATCTTTTTC CCTTCTTTTG TTCAGTTTTC AGAGGTTTCAT 60

CTCTCAAAAC GTGTTCTTTG AAAACTAGAT AAGAAAAGTT AGTGTAAGAAA GACGAAGAGA 120

AACCGTAGGT TTTTCTTCAA CCAAAACCGA GAATCAAACC GAGAAAGAAT CTTCCGTTT 180

TCATAAGCGA TCGCACGTTT ATGAAAACAC AACAACACCT TCGTAAGAAG GATGA 235

(2) INFORMATION FOR SEQ ID NO: 214:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 475 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 214:

TAAGGATAAG GAAACCTGTG AATCTTTTTC CCTTCTTTTG TTCAGTTTTC AGAGGTCAAT 60

GACGCTCATA CTGAGTACCA GGTGACACGT TTTTGAGGTG TCTCTTCGTA TGAGGGGCCT 120

ATAGCTCAGC TGGTTAGAGC GCACGCCTGA TAAGCGTGAG GTCGGTGGTT CGAGTCCACT 180  
 5 TAGGCCCACT TTTTGAATA AACCTTCTT TTTTATATGT TAATAAGGGG CCTTAGCTCA 240  
 GCTGGGAGAG CGCCTGCTTT GCACGCAGGA GGTGAGCGGT TCGATCCCGC TAGGCTCCAC 300  
 CAAAGATAGT TTGTTCTTTG AAAACTAGAT AAGAAAAGTT AGTGTAAGAA GACGAAGAGA 360  
 10 AACCGTAGGT TTTTCTTCAA CAAAACCGA GAATCAAACC GAGAAAGAAT CTTCCGTTT 420  
 TCATAAGCGA TCGCACGTTT ATGAAAACAC AACAACACCT TCGTAAGAAG GATGA 475

## (2) INFORMATION FOR SEQ ID NO: 215:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 463 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 215:

30 TAAGGATAAG GAAACCTGTG AATCTTTTTC CCTTCTTTTG TTCAGTTTGT AGAGGTCAAT 60  
 GACGCTCATA CTGAGTACCA GGTGACACGT TTTTGAGGTG TCTCTTCGTA TGAGGGGCCT 120  
 ATAGCTCAGC TGGTTAGAGC GCACGCCTGA TAAGCGTGAG GTCGGTGGTT CGAGTCCACT 180  
 35 TAGGCCCACT TTTTGAATA AACCTTCTT TTTTATATGT TAATAAGGGG CCTTAGCTCA 240  
 GCTGGGAGAG CGCCTGCTTT GCACGCAGGA GGTGAGCGGT TCGATCCCGC TAGGCTCCAC 300  
 CAAAGATAGT TTGTTCTTTG AAAACTAGAT AAGAAAAGTT AGTGTAAGAA GACGAAGAGA 360  
 40 AACCGTAGGT TTTTCTTCAA CAAAACCGA GAAAGAATCT TTCCGTTTTC ATAAGCGATC 420  
 GCACGTTTAT GAAAACACAA CAACACCTTC GTAAGAAGGA TGA 463

## (2) INFORMATION FOR SEQ ID NO: 216:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 19 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 216:

TGGCCGGTGC AAAGGGCTG

19

10

## Claims

15 1. Method for the detection and identification of at least one strain of Staphylococcus species or for the simultaneous detection of several microorganisms of which at least one strain of Staphylococcus species in a sample, comprising the steps of:

- 20 (i) releasing, isolating and/or concentrating the polynucleic acids from the micro-organism(s) to be detected in the sample;  
 (ii) if need be amplifying the 16S-23S rRNA spacer region, or a part of it, from the micro-organism(s) to be detected, with at least one suitable primer pair;  
 (iii) hybridizing the polynucleic acids of step (i) or (ii) to at least one of the following probes:

25 STAU-ICG 1 : TACCAAGCAAAACCGAGTGAATAAAGAGTT (SEQ ID NO 53)  
 STAU-ICG 2 : CAGAAGATGCGGAATAACGTGAC (SEQ ID NO 54)  
 STAU-ICG 3 : AACGAAGCCGTATGTGAGCATTGAC (SEQ ID NO 55)  
 30 STAU-ICG 4 : GAACGTAACCTTCATGTTAACGTTTGACTIONTAT (SEQ ID NO 56)

or to equivalents of said probes,  
 and/or to any probe derived from SEQ ID NO 139, 140, 141, 142, 143 or 144 provided said probe hybridizes specifically to Staphylococcus species;  
 35 (iv) detecting the hybrids formed in step (iii);  
 (v) identification of the micro-organism(s) present in the sample from the differential hybridization signals obtained in step (iv).

40 2. Method according to claim 1 to detect and identify one or more Staphylococcus aureus strains, wherein step (iii) comprises hybridizing to at least one, and preferably both of the following probes:

STAU-ICG 3 : AACGAAGCCGTATGTGAGCATTGAC (SEQ ID NO 55)  
 45 STAU-ICG 4 : GAACGTAACCTTCATGTTAACGTTTGACTIONTAT (SEQ ID NO 56),

or to equivalents of said probes,  
 and/or to any probe derived from SEQ ID NO 139, 140, 141, 142 or 143 provided said probe hybridizes specifically to Staphylococcus aureus.

50

3. Method according to claim 1 to detect and identify one or more Staphylococcus epidermidis strains in a sample, wherein step (iii) comprises hybridizing to any probe derived from SEQ ID NO 144 provided said probe hybridizes specifically to Staphylococcus epidermidis.

55 4. Method according to claim 1 wherein step (iii) is further characterized that the polynucleic acids of step (i) or (ii) are hybridized with a set of probes comprising at least two probes under the same hybridization and wash conditions, with said probes being selected from the sequences of table 1a or equivalents thereof, and/or from taxon-specific probes derived from any of the spacer sequences as represented in figures 1-103, with said taxon-specific

probe being selected such that it is capable of hybridizing under the same hybridization and wash conditions as at least one of the probes of table 1a.

5. Method according to claim 4, wherein the sample is originating from the respiratory tract and wherein step (iii) is further characterized that the set of probes comprises at least one probe chosen from the following spacer probes:

MYC-ICG-1 :	ACTGGATAGTGGTTGCGAGCATCTA	(SEQ ID NO 1)
MYC-ICG-22 :	CTTCTGAATAGTGGTTGCGAGCATCT	(SEQ ID NO 2)
MTB-ICG-1 :	GGGTGCATGACAACAAAGTTGGCCA	(SEQ ID NO 3)
MTB-ICG-2 :	GACTTGTTCCAGGTGTTGTCCCAC	(SEQ ID NO 4)
MTB-ICG-3 :	CGGCTAGCGGTGGCGTGTTCT	(SEQ ID NO 5)
MAI-ICG-1 :	CAACAGCAAATGATTGCCAGACACAC	(SEQ ID NO 6)
MIL-ICG-11 :	GAGGGGTTCCCGTCTGTAGTG	(SEQ ID NO 7)
MIL-ICG-22 :	TGAGGGGTTCTCGTCTGTAGTG	(SEQ ID NO 8)
MAC-ICG-1 :	CACTCGGTCGATCCGTGTGGA	(SEQ ID NO 9)
MAV-ICG-1 :	TCGGTCCGTCCGTGTGGAGTC	(SEQ ID NO 10)
MAV-ICG-22 :	GTGGCCGGCGTTCATCGAAA	(SEQ ID NO 11)
MIN-ICG-1 :	GCATAGTCCTTAGGGCTGATGCGTT	(SEQ ID NO 12)
MIN-ICG-2 :	GCTGATGCGTTCGTCGAAATGTGTA	(SEQ ID NO 13)
MIN-ICG-22 :	CTGATGCGTTCGTCGAAATGTGT	(SEQ ID NO 14)
MIN-ICG-222 :	TGATGCGTTCGTCGAAATGTGT	(SEQ ID NO 15)
MIN-ICG-2222 :	GGCTGATGCGTTCGTCGAAATGTGTAA	(SEQ ID NO 16)
MAL-ICG-1 :	ACTAGATGAACGCGTAGTCCTTGT	(SEQ ID NO 17)
MHEF-ICG-1 :	TGGACGAAAACCGGGTGACAA	(SEQ ID NO 18)
MAH-ICG-1 :	GTGTAATTTCTTTTAACTCTTGTGTGTAAGTAAGTG	

		(SEQ ID NO 19)
	MCO-ICG-11 : TGGCCGGCGTGTTTCATCGAAA	(SEQ ID NO 20)
5	MTH-ICG-11 : GCACTTCAATTGGTGAAGTGCGAGCC	(SEQ ID NO 21)
	MTH-ICG-2 : GCGTGGTCTTCATGGCCGG	(SEQ ID NO 22)
	MEF-ICG-11 : ACGCGTGGTCCTTCGTGG	(SEQ ID NO 23)
10	MSC-ICG-1 : TCGGCTCGTTCTGAGTGGTGTC	(SEQ ID NO 24)
	MKA-ICG-1 : GATGCGTTTGCTACGGGTAGCGT	(SEQ ID NO 25)
	MKA-ICG-2 : GATGCGTTGCCTACGGGTAGCGT	(SEQ ID NO 26)
15	MKA-ICG-3 : ATGCGTTGCCCTACGGGTAGCGT	(SEQ ID NO 27)
	MKA-ICG-4 : CGGGCTCTGTTGAGAGTTGTC	(SEQ ID NO 28)
	MKA-ICG-5 : CCCTCAGGGATTTCTGGGTGTTG	(SEQ ID NO 182)
20	MKA-ICG-6 : GGACTCGTCCAAGAGTGTTGTCC	(SEQ ID NO 183)
	MKA-ICG-7 : TCGGGCTTGCCAGAGCTGTT	(SEQ ID NO 184)
	MKA-ICG-8 : GGGTGCGCAACAGCAAGCGA	(SEQ ID NO 185)
25	MKA-ICG-9 : GATGCGTTGCCCCCTACGGG	(SEQ ID NO 186)
	MKA-ICG-10 : CCCTACGGGTAGCGTGTTCTTTTG	(SEQ ID NO 187)
	MCH-ICG-1 : GGTGTGGACTTTGACTTCTGAATAG	(SEQ ID NO 29)
30	MCH-ICG-2 : CGGCAAAACGTCGGACTGTCA	(SEQ ID NO 30)
	MCH-ICG-3 : GGTGTGGTCCTTGACTTATGGATAG	(SEQ ID NO 210)
	MGO-ICG-1 : AACACCCTCGGGTGCTGTCC	(SEQ ID NO 31)
35	MGO-ICG-2 : GTATGCGTTGTCGTTGCGGGC	(SEQ ID NO 32)
	MGO-ICG-5 : CGTGAGGGGTCATCGTCTGTAG	(SEQ ID NO 33)
	MUL-ICG-1 : GGTTTCGGGATGTTGTCCCACC	(SEQ ID NO 175)
40	MGV-ICG-1 : CGACTGAGGTCGACGTGGTGT	(SEQ ID NO 176)
	MGV-ICG-2 : GGTGTTTGAGCATTGAATAGTGGTTGC	(SEQ ID NO 177)
	MGV-ICG-3 : TCGGGCCGCGTGTTTCGTCAAA	(SEQ ID NO 211)
45	MXE-ICG-1 : GTTGGGCAGCAGGCAGTAACC	(SEQ ID NO 178)
	MSI-ICG-1 : CCGGCAACGGTTACGTGTTT	(SEQ ID NO 179)
	MFO-ICG-1 : TCGTTGGATGGCCTCGCACCT	(SEQ ID NO 180)
50	MFO-ICG-2 : ACTTGGCGTGGGATGCGGGAA	(SEQ ID NO 181)
	MML-ICG-1 : CGGATCGATTGAGTGCTTGTCCT	(SEQ ID NO 188)
	MML-ICG-2 : TCTAAATGAACGCACTGCCGATGG	(SEQ ID NO 189)
55	MCE-ICG-1 : TGAGGGAGCCCGTGCCTGTA	(SEQ ID NO 190)

	MHP-ICG-1 :	CATGTTGGGCTTGATCGGGTGC	(SEQ ID NO 191)
	PA-ICG 1 :	TGGTGTGCTGCGTGATCCGAT	(SEQ ID NO 34)
5	PA-ICG 2 :	TGAATGTTTCGTGGATGAACATTGATT	(SEQ ID NO 35)
	PA-ICG 3 :	CACTGGTGATCATTCAAGTCAAG	(SEQ ID NO 36)
	PA-ICG 4 :	TGAATGTTTCGT(G/A)(G/A)ATGAACATTGATTTCTGGTC	
10			(SEQ ID NO 37)
	PA-ICG 5 :	CTCTTTCCTGCTGGTGATCATTCAAGTCAAG	(SEQ ID NO 38)
	MPN-ICG 1 :	ATCGGTGGTAAATTAAACCCAAATCCCTGT	(SEQ ID NO 49)
15	MPN-ICG 2 :	CAGTTCTGAAAGAACATTTCCGCTTCTTTC	(SEQ ID NO 50)
	MGE-ICG 1 :	CACCCATTAATTTTTTCGGTGTTAAACCC	(SEQ ID NO 51)
	Mycoplasma-ICG :	CAAACTGAAAACGACAATCTTTCTAGTTCC	(SEQ ID NO 52)
20	STAU-ICG 1 :	TACCAAGCAAAACCGAGTGAATAAAGAGTT	(SEQ ID NO 53)
	STAU-ICG 2 :	CAGAAGATGCGGAATAACGTGAC	(SEQ ID NO 54)
	STAU-ICG 3 :	AACGAAGCCGTATGTGAGCATTTGAC	(SEQ ID NO 55)
25	STAU-ICG 4 :	GAACGTAACCTTCATGTAAACGTTTGACTTAT	(SEQ ID NO 56)
	ACI-ICG 1 :	GCTTAAGTGCACAGTGCTCTAAACTGA	(SEQ ID NO 57)
30	ACI-ICG 2 :	CACGGTAATTAGTGTGATCTGACGAAG	(SEQ ID NO 58)

or equivalents of said probes,

and/or wherein the set of probes comprises at least one taxon-specific probe derived from the spacer region sequence corresponding to one of the micro-organisms to be detected in said sample, said spacer region sequence being chosen from any of the sequences as represented by SEQ ID NO 76 to 106, 157 to 174, 124, 125, 111 to 115, 139 to 144, or 126 to 130,

and with said probes or equivalents being possibly used in combination with any probe detecting at least one of the following organisms: Haemophilus influenzae, Streptococcus pneumoniae, Moraxella catarrhalis or Bordetella pertussis.

6. Method according to claim 4, wherein the sample is originating from food, and wherein the set of probes as defined in step (iii) comprises at least one probe chosen from the following spacer probes:

45	LIS-ICG 1 :	CAAGTAACCGAGAATCATCTGAAAGTGAATC	(SEQ ID NO 39)
	LMO-ICG 1 :	AAACAACCTTTACTTCGTAGAAGTAAATTGGTTAAG	
			(SEQ ID NO 40)
50	LMO-ICG 2 :	TGAGAGGTTAGTACTTCTCAGTATGTTTGTTTC	(SEQ ID NO 41)

55

LMO-ICG 3 : AGGCACTATGCTTGAAGCATCGC (SEQ ID NO 42)

LIV-ICG 1 : GTTAGCATAAATAGGTAAGTATTTATGACACAAGTAAC

(SEQ ID NO 43)

LSE-ICG 1 : AGTTAGCATAAGTAGTGTAAGTATTTATGACACAAG (SEQ ID NO 44)

LISP-ICG 1 : CGTTTTTCATAAGCGATCGCACGTT (SEQ ID NO 212)

STAU-ICG 1 : TACCAAGCAAAACCGAGTGAATAAAGAGTT (SEQ ID NO 53)

STAU-ICG 2 : CAGAAGATGCGGAATAACGTGAC (SEQ ID NO 54)

STAU-ICG 3 : AACGAAGCCGTATGTGAGCATTTGAC (SEQ ID NO 55)

STAU-ICG 4 : GAACGTAACTTCATGTAAACGTTTGACTTAT (SEQ ID NO 56)

BRU-ICG 1 : CGTGCCGCCTTCGTTTCTCTTT (SEQ ID NO 59)

BRU-ICG 2 : TTCGCTTCGGGGTGGATCTGTG (SEQ ID NO 60)

BRU-ICG 3 : GCGTAGTAGCGTTTGCCTCGG (SEQ ID NO 193)

BRU-ICG 4 : CGCAAGAAGCTTGCTCAAGCC (SEQ ID NO 194)

SALM-ICG 1 : CAAAACTGACTTACGAGTCACGTTTGAG (SEQ ID NO 61)

SALM-ICG 2 : GATGTATGCTTCGTTATTCCACGCC (SEQ ID NO 62)

STY-ICG 1 : GGTCAAACCTCCAGGGACGCC (SEQ ID NO 63)

SED-ICG 1 : GCGGTAATGTGTGAAAGCGTTGCC (SEQ ID NO 64)

YEC-ICG 1 : GGAAAAGGTACTGCACGTGACTG (SEQ ID NO 198)

YEC-ICG 2 : GACAGCTGAAACTTATCCCTCCG (SEQ ID NO 199)

YEC-ICG 3 : GCTACCTGTTGATGTAATGAGTCAC (SEQ ID NO 200)

or equivalents of said probes,

and/or wherein the set of probes comprises at least one taxon-specific probe derived from the spacer region sequence corresponding to one of the micro-organisms to be detected in said sample, said spacer region sequence being chosen from any of the sequences as represented by SEQ ID NO 116, 117, 118-121, 213-215, 139-144, 131, 132, 154, 133-138, 195 or 196,

with said probes or equivalents being possibly used in combination with any probe detecting strains of Campylobacter species.

7. Composition comprising at least one of the probes as defined in claims 1 to 3.

8. Probe as defined in any of claims 1 to 3.

9. Reverse hybridization method according to any of claims 1 to 6 wherein the probes are immobilized on a known location on a solid support, more preferably on a membrane strip.

10. Kit for the detection and identification of at least one strain of Staphylococcus species, or the simultaneous detection and identification of several micro-organisms of which at least one strain of Staphylococcus species in a sample, comprising the following components:

(i) when appropriate, at least one suitable primer pair to allow amplification of the 16S-23S rRNA spacer region, or a part of it;



- (ii) at least one of the probes as defined in claim 8;  
(iii) a buffer, or components necessary to produce the buffer, enabling a hybridization reaction between said probes and the polynucleic acids present in the sample, or the amplified products thereof;  
(iv) a solution, or components necessary for producing the solution, enabling washing of the hybrids formed under the appropriate wash conditions;  
(v) when appropriate, a means for detecting the hybrids resulting from the preceding hybridization.

5

10

15

20

25

30

35

40

45

50

55

Figure 1

AAGGAGCACC ACGAAAACGC CCCAACTGGT GGGCGGTAGG CCGTGAGGGG TTCTTGTCTG TAGTGGGCGA  
GAGCCGGGTG CATGACAACA AAGTTGGCCA CCAACACACT GTTGGGTCCT GAGGCAACAC TCGGACTTGT  
TCCAGGTGTT GTCCCACCGC CTTGGTGGTG GGGTGTGGTG TTTGAGAACT GGATAGTGGT TCGGAGCATC  
AATGGATACG CTGCCGGCTA GCGGTGGCGT GTTCTTTGTG CAATATTCTT TGGTTTTTGT TGTGT

(SEQ ID NO 76)

Figure 2

AAGGAGCACC ACGAAAAGCA CCCCAACTGG TGGGGTGCGA GCCGTGAGGG GTTCCCCTCT GTAGTGGACG  
GGGGCCGGNT GCGCAACAGC AATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCCCCTC  
CGTGTGGAGT CCTCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGAGCGCA TGGTCTTCGT GGCCGGCGTT CATCGAAATG TGTAAATTTCT TCCTTAACTC TTGTGTGT

(SEQ ID NO 77)

Figure 3

AAGGAGCACC ACGAAAAGCA CCCCAACTGG TGGGGTGCGA GCCGTGAGGG GTTCCCCTCT GTAGTGACG  
GGGGCCGGGT GCGCAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGTCCGTC  
CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGAGCGCA TGGTCTTCGT GGCCGGCGTT CATCGAAATG TGTAAATTCT TTTTAACTC TTGTGTGT

(SEQ ID NO 78)

Figure 4

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCCCCTCT GTAGTGGACG  
GGGGCCGGNT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCGATC  
CGTGTGGAGT CCTCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGAGCGCA TAGTCCTTGT GGCTGATGCG CTCGTCGAAA TGTGTAATTT CTTCTTTGGT GTNTGTGTGT

(SEQ ID NO 79)

Figure 5

AAGGAGCACC ACGAAAAGCA TCCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
AAACCGGGT GCACAAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAAACAC TCGGTCGATC  
CGTGTGGAGT CCTCCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGAGCGCG TAGTCCTTTG TGGCTGATGC GTTCATCAAA ATGTGTAATT TCTTTTGG TTTNTGTGTG  
T

(SEQ ID NO 80)

Figure 6

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCCCCTCT GTAGTGGACG  
GGGGCCGGGT GCACAACAGC AATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCGATC  
CGTGTGGAGT CCCGCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGAGCGCA TAGCCCTTGC GGCTGATGCG TTCGNCGAAA TGTGTAATTT CTTCTCTGGT TTCTGTGTGT

(SEQ ID NO 81)

Figure 7

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
 GNAGCCGGGT GCACAACAGC AATGATTGC CAGACACACT ATTGGGCCCTT GAGACAACAC TCGGTCGATC  
 CGTGTGGAGT CCTCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
 GATGAGCGCG TAGTCCTTCG TGGCTGATGC GTTCATCGAA ATGTGTAATT TCTTCTTTGG TTTTGGGGTGT  
 GT

(SEQ ID NO 82)



Figure 8

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCCCCTCT GTAGTGGACG  
GGGGCCGGGT GCACAACAGC AAATGATCGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCGATC  
CGTGTGGAGT CCTCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGAGCGCA TAGTCCTTTG GGGCTGATGT GTTTCATCAA AATGTGAAT TTCCTTTTNG GTTTTNGTGT  
GT

(SEQ ID NO 83)

Figure 9

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
GGAGCCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCGATC  
CGTGTGGAGT CCTCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGAGCGCG TAGTCCTTCG TGGCTGATGC GTTCATTGAA ATGTGTAATT TCTTCTCTGG TTTTGTGTG  
T

(SEQ ID NO 84)

Figure 10

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCCCCTCT GTAGTGGACG  
GGGGCCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCGATC  
CGTGTGGAGT CCTCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGAGCGCA TAGTCCTTGT GGCTGATGCG CTCGTCGAAA TGTGTAATTT CTTCTTTGGT TTTTGTGTGT

(SEQ ID NO 85)

Figure 11

AAGGAGCAC CACGAAAAGCA CTCCAATTGG TGGGTGCGA GCCGTGAGG GTTCCCCGTCT GTAGTGGACG  
GGGGCCGGGT GCGCAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCGATC  
CGTGTGGAGT CCTCCATCT TGGTGGTGGG GTGTTGGTGT TTGAGTATTG GATAGTGTT GCGAGCATCT  
AGATGAGCGC GTAGTCCTTG TGGCTGATGC GTTCGTCGAA ATGTGTAATT TCTTCTTTGG GTTTTGTGT  
GT

(SEQ ID NO 86)

Figure 12

AAGGAGCACC ACGAAAAGCA CCCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
GNAGCCGENT GCGCAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGNCGATC  
CGTGTGGAGT CCTCCATCT TGGTGGTGGG GTGTNGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGGGCGCG TAGTCCTTTG TGACTGATGC GTTCATCAAA ATGTGTAATT TCTTTTTCN NTTTNGTGTG  
T

(SEQ ID NO 87)

Figure 13

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTCCGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
GGAACCGGGT GCACAACAGC AATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCGATC  
CGTGTGGAGT CCTCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGAGCGCA TAGTCCTTG TGGCTGACGC GTTCATCGAA ATGTGTAATT TCTTCTTTGG TTTTGTGTG  
T

(SEQ ID NO 88)

Figure 14

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGTGANGG GTTCCCCTCT GTAGTGGACG  
GGGGCCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCGATC  
CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGGT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGAGCGCA TAGTCCTTAG GGCTGATGCG TTCGTCGNAA TGTGTAATTT CTTCTTTGGT TTTTGTGTGT

(SEQ ID NO 89)

Figure 15

AAGGAGCACC ACGAAAAGCA TCCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
AAAACCGGGT GCACAACAGC AATAAATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCGATC  
CGTGTGGTGT CCTCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGTTG CGAGCATCTA  
GATGAACGCG TAGTCCTTCG TGGCTGACGT GTTCATCGAA ATGTGTAATT TCTTNTNTTA ACTCTTGTGT  
GT

(SEQ ID NO 90)



Figure 16

AAGGAGCAC ACGAAAAGCA CCCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
GGAGCCGGGT GCACAACAGC AATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCAGTC  
CGTGTGGTGT CCTCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGAACGCG TAGTCCCTGT GACTGACGTG TTCATCGAAA TGTGTAATTT CTTTCTAAC TCTTGTGTGT

(SEQ ID NO 91)

Figure 17

AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
AAAGCCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAAAC TCGGTCGAAC  
CGTGTGGAGT CCTCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGAACGCG TGGTCTTCAT GGCCGGCGTG TTCATCGAAA TGTGTAATAT CTTCTCTGGT TTTCGGGTGTG  
T

(SEQ ID NO 92)

Figure 18

AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
AAAACCGGNT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCGATC  
CGTGTGGAGT CCTCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGAACGCG TGGTCTTCAT GGCCGGCGTG TTCATCGAAA TGTGTAATTT CTTTNNAC TCTTGTGTGT

(SEQ ID NO 93)

Figure 19

AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
AAAGCCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCGAAC  
CGTGTGGAGT CCTCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGAACGG TGGTCTTCAT GGCCGGCGTG TTCATCGAAA TGTGTAATT CTTCCTTTGGT TTTNGTGTGT

(SEQ ID NO 94)

Figure 20

AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
AAAACCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCGATC  
CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGAACGCG TAGTCCTTCG NGGNCNGCGT GTTCATCGAA ATGTGTAATT TCNTTNTTAA CTCNNGTGTG  
T

(SEQ ID NO 95)

Figure 21

AAGGAGCACC ACGAAAAGCA TCCCAATTGG TGGGGTGTGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
AAAACCGGGT GCACAACAGC AATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCGATC  
CGTGTGGAGT CCTCCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGAACGCG TAGTCCTTCG GGGCCGGCGT GTTCATCGAA ATGTGTAATT TCTTTTTTAA CTCTTGTGTG  
T

(SEQ ID NO 96)

Figure 22

AAGGAGCACC ACGAAAAGCA CTTCANTTGG TGAAGTGCGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
AAACCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCGAAC  
CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGTTG CGAGCATCTA  
GATGAACGCG TGGTCTTCAT GGCCGGCGTG TTCATCGAAA TGTGTAATT CTTCCTTAAC TCTTGTGTGT

(SEQ ID NO 97)

Figure 23

AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
AAAACCGGGT GCACAACAGN AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCGATC  
CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGAACGCG TGGTCTTCAT GGCCNGCGTG TTCATCGAAA TGTGTAATTT CTTTTTTAAC TCTTGTGTGT

(SEQ ID NO 98)



Figure 24

AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
AAAACCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCGATC  
CGTGTGGAGT CCTCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
GATGAACGCG TGGTCTTCAT GGCCGGCGTG TTCATCGAAA TGTGTAATTT CTTTTTAAC TCTTGTGTGT

(SEQ ID NO 99)

Figure 25

AAGGAGCACC ACGAAAAGCA CCCCAACTGG TGGGGTGCGA GCCGTGAGGG GTCCCTCGCCT GTAGTGGGCG  
GGGGCCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGGCAACAC TCGGCTCGTT  
CTGAGTGGTG TCCCTCCATC TTGGTGGTGG GGTGTGGTGT TTGAGTATTG GATAGTGGTT GCGAGCATCT  
AAACGGATGC GTGGCCGGCA ACGGTGGCGT GTTCGTTGAA ATGTGTAATT TCTTTTTTGG TTTTGTGTG  
T

(SEQ ID NO 100)

Figure 26

AAGGAGCACG ACGAAAAGCA TCCCAACAAG TGGGGTGCAA NCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
AAAGCCGGGT GCACGACAAC AAGCAAAGCC AGACACACTA TTGGGTCCTG AGGCAACACT CCGGCTCTGT  
TCGAGAGTTG TCCCACCATC TTGGTGGTGG GGTGTGTTGT TTGAGAAATTG GATAGTGTT GCGAGCATCA  
AATGGATGCG TTGCCCTACG GGTAGCGTGT TCTTTTGTGC AATTTATTTC TTTGGTTTTT GTGT

(SEQ ID NO 101)

Figure 27

AAGGAGCACC ATTTCCAGT CGATGAACTA GGGAACATAA AGTAGGCATC TGTAGTGGAT ATCTACTTGG  
TGAATATGTT TTGTAAATCC TGTCACACCC GTGGATGGGT AGTCGGCAAA ACGTCGGACT GTCATAAGAA  
TTGAAACGGT GGCACACTGT TGGGTCCTGA GGCAACACGT TGTGTTGTCA CCTGCTTGG TGGTGGGGTG  
TGGACTTTGA CTTCTGAATA GTGGTTGCCA GCATCTAAAC ATAGCCTCGC TCGTTTTTCGA GTGGGGGCTGG  
TTTGTGAATT TTA

(SEQ ID NO 102)

Figure 28

AAGGAGCACC ATTTCCCACT CGGATGAACT AGGGAACATA AAGTAGGCAT CTGTAGTGGG TATCTACTTG  
GTGAATATGT TTTGTAATC CTGTCCACCC CCGTGGATGG GTAGTCGGCA AAACGTCGGA CTGTCATAAG  
AATTGAAACG CTGGCACACT GTTGGGTCCT GAGGCAACAC GTTGTGTTGT CACCCCTGCTT GGTGGTGGGG  
TGTTGGACTTT GACTTCTGAA TAGTGGTTGC GAGCATCTAA ACATAGCCTC GCTCGTTTTC GAGTGAGGCT  
GGTTTTTGCA ATTTTA

(SEQ ID NO 103)

Figure 29

AAGGAGCACC ACGAAGAGCA CTCCAATTGG TGGGTGCCGA GCCGTGAGGG GTCATCGTCT GTAGTGGACG  
AAGACCGGGT GCACGACAAC AAGCTAAGCC AGACACACTA TTGGGTCCCTG AGGCAACACC CTCGGGTGCT  
GTCCCCCCAT CTTGGTGGTG GGGTGTGGTG TTTGAGAATT GGATAGTGGT TGGGAGCATC AAAATGTATG  
CGTTGTCGTT CTCGGCAACG TGTCTTTTT GTGCAATTTA TTCTTTGGTT TTTGTAGTGT TTGT

(SEQ ID NO 104)

Figure 30

AAGGAGCACC ACGAAGAGCA CTCCAATTGG TGGGGTGCGA GCCNGAGGG GTCATCGTCT GTAGTGGACG  
AAGACTGGGT GCACGACAAC AAAGCAAGCC AGACACACTA TTGGGTCCCTG AGGCAACACC CTCGGGTGCT  
GCCCTCCAT CTGGTGGTG GGGTGTGGTG TTTGAGAACT GGATAGTGGT TCGGAGCATC AAAAATGTAT  
GCGTTGTCGT TCGCGACAAC GTGTTCTTTT TGTGCAATTT TAAATCTTTT GGTTTGGTA GTGTTTGT

(SEQ ID NO 105)

Figure 31

AAGGAGCACC ACGAGAAGCA CTCCAATTGG TGGGGTGCAA GCCGTGAGGG GTCATCGTCT GTAGTGGACG  
AAGACCGGGT GCACGACAAC AAGCAAAGCC AGACACACTA TTGGGTCCCTG AGGCAACACC CTCGGGTGCT  
GTCCCCCCAT CTTGGTGGTG GGGTGTGGTG TTTGAGAACT GGATAGTGGT TGGGAGCATC AAAATGTATG  
CGTGTGCGTT CGCGGCAACG TGTCTTTTT GTGCAATTTT TATTCITTGG TTTTGTAGT GTTTGT

(SEQ ID NO 106)



Figure 32

AAGGAGCACC ACGAAAAGCA CCCCAATTGG TGGGGTGCAA GCCGTGAGGG GTTCCCGCCT GTAGTGGGCG  
GGGCCGGGTG CGCAACAGCA AATGATTGCC AGACACACTA TTGGGCCCTG AGGCAACACT CGGATCGATT  
GAGTGCTTGT CCCCCCATCT TGGTGGTGGG GTGTGGTGTT TGAGAACTGG ATAGTGGTTG CGAGCATCTA  
AATGAACGCA CTGCCGATGG TGGTGTGTTT GTTTTGTA ATTTATTCT TTGGTTTTTG TGTTTGT

(SEQ ID NO 107)

Figure 33

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGTNAGGG GTTCTCGTCT GTAGTGGATG  
GCAGCCGGGT GCACANCAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCAGTC  
CGTGTGGAGT CCTCCATCT TGGTGGTGGG GTGTGGNGTT TGAGTATTGG ATAGTGGTTG CGANCACTCTA  
GATGAACGCG TAGTCCTCNG TGGCTGACGT GTTCATCAAA ATGTGTAAAT TCTTTTANGG GTTTNGGTGT  
CT

(SEQ ID NO 108)

Figure 34

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCNGAGGG GTTCTCGCCT GTAGTGGNCG  
AGGGCCGGAT GCACAACAAC ACATGATTGC CAGACACACT ATTGGGCCCT GANACAACAC TCGGCCAGTC  
CGTGTGGTGT CCTCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATNGG ATAGTNGTTG NGANCACTTA  
AACGGCTGCG TNGNCNGAA CCGTGGCCGTG TTCGNTAAAA TGTGTAATTT CTTTNNNGGT TTGGGTGTNT

(SEQ ID NO 109)

Figure 35

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCGA GCCGTGAGGG GTTCTCGCCT GTAGTGGGCG  
ANGGCCGGGT GCACAACAAC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGCCAGTC  
CGTGTGGTGT CCNCCATCT TGGTGGTGGG GTGTGGTGTT TGAGTATTGG ATAGTGGTTG CGAGCATCTA  
AANGGNTGCG TTGCCGNNAN CNGTGGCGTN TTCGNTAAAA TGTGTAANTT CTTTTTNGGT TTGTGTGTGT

(SEQ ID NO 110)

Figure 36

ATCGAAGATC CCGGCTTCTT CATAAGCTCC CACACGAATT GCTTGATTCA CTGTTAGAC GATTGGGTCT  
GTAGCTCAGT TGGTTAGAGC GCACCCCTGA TAAGGGTGAG GTCGGCAGTT CGAATCTGCC CAGACCCACC  
AATTGTTGGT GTGCTGCGTG ATCCGATACG GGGCCATAGC TCAGCTGGGA GAGCGCCTGC TTTGCCACGCA  
GGAGGTCAGG AGTTCGATCC TCCTTGGCTC CACCATCTAA AACAAATCGTC GAAAGCTCAG AAATGAATGT  
TCGTGGATGA ACATTGATTT CTGGTCTTTG CACCAGAACT GTTCTTTAAA AATTCGGGTA TGTGATAGAA  
GTAAGACTGA ATGATCTCTT TCACTGGTGA TCATTCAAGT CAAGGTAAAA TTTGCGAGTT CAAGCGCGAA  
TTTTCGGCGA ATGTCGTCTT CACAGTATAA CCAGATTGCT TGGGGTTATA T

(SEQ ID NO 111)

Figure 37

ATCGAAGACA TCAGCTTCTT CATAAGTATC CACACGAATT GCTTGATTCA TAGTGAACG AATGCTGTAA  
CGCGACCCGT GTTATAGGTC TGTAAGCTCAG TTGGTTAGAG CGCACCCCTG ATAAGGTGA GGTCGGCAGT  
TCAAAATCTGC CCAGACCTAC CAATTGCTTG GTCGAGAAAGA ATACGGGGCC ATAGCTCAGC TGGGAGAGCG  
CCTGCCCTTG ACGCAGGAGG TCAGCGGCTC GATCCCGCTT GGCTCCACCA CTCTCTCGTG TTGCGGTGAG  
TGTTAAAGAG TTCAGAAATG ATGCCGCTTC AGGTTTGTC TGTGAGTGC TGATTTCTGG TCTTTTGACC  
GGTACGAAAA TCGTTCTTTA AAAATTGGA TATGTGATAG AAGTGACTGA TTAATTGCTT TCACTGGCAA  
TTGATCTGGT CAAGGTAAAA TTTGTAGTTC TCAAGACGCA AATTTTCGGC GAATGTCGTC TTCACGATTG  
AGACAGTAAC CAGATTGCTT GGGGTTATAT

(SEQ ID NO 112)

Figure 38

ATCGAAGACA CCGGCTTCGT CATAAGCTCC CACACGAATT GCTTGATTCA CTTCGAAAG GCGATTGGGT  
TTAGACCCGA GAGTAACGAT TGGTCTGTA GCTCAGTTGG TTAGAGCGCA CCCCTGATAA GGGTGAGGTC  
GGCAGTTTGA ATCTGCCAG ACCCACCAAT CGAAGGGCC ATAGCTCAGC TGGGAGAGCG CCTGCTTTGC  
ACGCAGGAGG TCAGCGGTTT GATCCCGCTT GGCTCCACCA TTAACCTCTAG TCGCCGAAAG CTCAGAAATG  
AGTGTTTACC AGGATGAGGT TGATTGCCCTG GGTGAACAT TGATTTCTGG ACTTTGCGCC AGAACTGTTC  
TTTAAAAAAT TGGGTATGT ATAGAAGTAG ACCGATGTGT TGCTTTCAC TGGCAGCATGT CGCGTCAAGG  
TAAAAATTGC GTGTTCTCTA TGCAAAATTT CGGCGAATGT CGTCTTCACG TTATAGACAG TAACCAGATT  
GCTTGGGGTT ATAT

(SEQ ID NO 113)

Figure 39

ATCGAAGACT TCAGCTTCTT CATAAGTTCC CACACGAATT GCTTGATTCA CTTGCGAAAA GCGATTGGGT  
TGAGACCCGA GAGTGACGAT TGGGTCTGTA GCTCAGTTGG TTAGAGCGCA CCCCTGATAA GGTGAGGTC  
GGCAGTTCGA ATCTGCCCAG ACCCACC AAT TGTGCGGATG GCCAGTGTCA AATGGGGCCA TAGCTCAGCT  
GGGAGAGCGC CTGCTTTGCA CGCAGGAGGT CAGGAGTTCC ATCCTCCTTG GCTCCACCAT CAACTCACGA  
TCGCTGAAAG CTCAGAAATG AACATTGGTA GTTCAATGTT GATTCTGGT CTTTGCGCCA GAACTGTTCT  
TTAAAAATTT GGGTATGTGA TAGAAGTGAC TAACAGCGTG TTTCACTGCA CGTTGTTAAT CAAGGCAAAA  
TTTGCGAGTT CAAGCGCGAA TTTTCGGCGA ATGTCGTCTT CACGTTACGA ATCTATAACC AGATTGCTTG  
GGTTATAT

(SEQ ID NO 114)



Figure 40

ATCGACGACA TCAGCTGTCT CATAAGCTCC CACACGAATT GCTTGATTCA TTGAAGAAGA CGATTAGGTT  
AGCAACCTTC GATTGGGTCT GTAGCTCAGT TGGTTAGAGC GCACCCCTGA TAAGGGTGAG GTCGGCAGTT  
CGAATCTGCC CAGACCCACC AATTGCTGG GGCCATAGCT CAGCTGGGAG AGCGCCTGCC TTGCACGCAG  
GAGGTCAGCG GTTCGATCCC GCTTGGCTCC ACCACCCCGC TTGCCAGTTT GTCAAAGCTT AGAAATGAAT  
ATTGCGGTCTG AATATTGATT TCTGAACTTT ATCAGAAATCG TTCTTTAAA ATTGCGGTAT GTGATAGAAA  
GATAGACTGG ACAGCACTTT CACTGGGTGT TGTTCAGGCT AAGGTAATAA TTGTGAGTAA TTACAAGTTT  
TCGGCGAATG TTGCTTCAC AGTATAACCA GATTGCTTGG GGTATAT

(SEQ ID NO 115)

Figure 41

TAAGGAAAAG GAAACCTGTG AGTTTTCGTT CTTCTCTGTT TGTTCAGTTT TGAGAGGTTA ATTCTTCTCT  
ATACTGTTTG TTCTTTGAAA ACTAGATAAG AAAGTTAGTA AAGTTAGCAT AATAGGTAA CTATTTATGA  
CACAAAGTAAC CGAGAATCAT CTGAAAAGTGA ATCTTTCATC TGATTGGAAG TATCATCGCT GATACGAAAA  
ATCAGAAAAA CAACCTTTAC TTCATCGAAG TAAATT

(SEQ ID NO 116)

Figure 42

CTAAGGAAAA GGAAACCTGT GAGTTTTCGT TCTTCTCTAT TTGTTCAAGT TTGAGAGGTT AGTACTTCTC  
AGTATGTTTG TTCTTTGAAA ACTAGATAAG AAAGTTAGTA AAGTTAGCAT AGATAATTTA TTATTTATGA  
CACAAAGTAAC CGAGAATCAT CTGAAAGTGA ATCTTTTCATC TGATTGGAAG TATCATCGCT GATACGGAAA  
ATCAGAAAAA CAACCTTTAC TTCGTAGAAG TAAATT

(SEQ ID NO 117)

Figure 43

TAAGGAAAAG GAAACCTGTG AGTTTTCGTT CTTCCTCTGTT TGAGAGGTTA TTACTTCTCT  
GTATGTTTGT TCTTTGAAAA CTAGATAAGA AAGTTAGTAA AGTTAGCATA AGTAGTGTA CTATTATGA  
CACAAAGTAAC CGAGAATCAT CTGAAAAGTGA ATCTTTCATC TAATTCGACG TATCATCGCT GATACAGACA  
ATTAGAAAAA CAACCTTTAC TTCGACGAAG TAAATT

(SEQ ID NO 118)

Figure 44

GGCCTATAGC TCAGCTGGTT AGAGCGCACG CCTGATAAGC GTGAGGTCGA TGGTTCGAGT CCATTTAGGC  
CCACTTTTTC TTTCTGACAG AAGAAACACT GTATAACCTA TTTAAGGGGC CTTAGCTCAG CTGGGAGAGC  
GCCTGCTTTG CACGCAGGAG GTCAGCGGTT CGATCCCGCT AGGCTCCACC AAAATTGTTC TTTGAAAACT  
AGATAAGAAA GTTAGTAAAG TTAGCATAAA TAGGTAACCTA TTTATGACAC AAGTAACCGA GAATCATCTG  
AAAGTGAATC TTTTCATCTGA TTGGAAGTAT CATCGCTGAT ACGAAAAATC AGAAAAACAA CCTTACTTC  
ATCGAAGTAA ATT

(SEQ ID NO 119)

Figure 45

TAAGGAAAAG GAAACCTGTG AGTTTTCGTT CTCTCTATT TGTTCAGTTT TGAGAGGTTA CTCTCTTTTA  
TGTCAGATAA AGTATGCAAG GCACTATGCT TGAAGCATCG CGCCACTACA TTTTGTGACGG GCCTATAGCT  
CAGCTGGTTA GAGCGCACGC CTGATAAGCG TGAGGTCGAT GGTTCGAGTC CATTTAGGCC CACTTTTCT  
TTC TGACATA AGAAATACAA ATAATCATA CTTTACGG GGCCTTAGCT CAGCTGGGAG AGCGCCTGCT  
TTGCACGCAG GAGGTCAGCG GTTCGATCCC GCTAGGCTCC ACCAAAATTG TTTCTTTGAAA ACTAGATAAG  
AAAGTTAGTA AAGTTAGCAT AGATAATTTA TTATTTATGA CACAAGTAAC CGAGAATCAT CTGAAAAGTGA  
ATCTTTCATC TGATTGGAAG TATCATCGCT GATACGGAAA ATCAGAAAAA CAACCTTTAC TTCGTAGAAG  
TAAATT

(SEQ ID NO 120)

Figure 46

TAAGGAAAAG GAAACCTGTN AGTTNCGTN CTTCTCTGTT TGTNCAGTTT TNAGAGGTTA CTCTCTTTNA  
TGTCAGATAA AGTACGCACG GCACGTTGCC TTGGGCAAG AGCCACTACA TTATTGACGG GCGTATAGCT  
CAGCTGGTTA GAGCGCACGC CTGATAAGCG TGAGGTCGAT GGTTCGAGTC CATTTAGGCC CACTTTTCT  
TTCTGACAGA AGAAATCATT TGCACATCCT ATTAATAAGG GNCCTTAGCT CAGCTGGGAG AGCGCCTGCT  
TTGCACGCAG GAGGTCAGCG GTTCGATCCC GCTAGGCTCC ACCCAAAATT GTTCTTTGAA AACTAGATAA  
GAAAGTTAGT AAAGTTAGCA TAAGTAGTAT AACTATTTAT GACACAAGTA ACCGAGAATC ATCTGAAAGT  
GAATCTTTCA TCTAATTCTGA CGTATCATCG CTGATACAGA CAATTNGAAA ACAACCTTT ACTTCGACGA  
AGTAAATT

(SEQ ID NO 121)

Figure 47

TAAGGATAAG GATAACTGTC TTAGGACGGT TTGACTAGGT TGGGCAAGCG TTTTTTTAAT CTTGTATTCT  
ATTCCTTTTG CATTGTTAAG CGTTGTTTCC AAAACATTTA GTTTACGATC AAGTATGTTA TGTAATAAAT  
ATGGTAACAA GTAAATTACAC ATATAATAAT AGACGTTTAA GAATATATGT CTTTAGGTGA TGTTAACTTG  
CATGGATCAA TAAATTACA

(SEQ ID NO 122)



Figure 48

TAAGGATAAG GAAGAAGCCT GAGAAGGTTT CTGACTAGGT TGGGCAAGCA TTTATATGTA AGAGCAAGCA  
TTCTATTTC A TTTGTGTTGT TAAGAGTAGC GTGGTGAGGA CGAGACATAT AGTTTGTGAT CAAGTATGTT  
ATTGTAAGA AATAATCATG GTAACAAGTA TATTCACGC ATAATAATAG ACGTTTAAAGA GTATTTGTCT  
TTTAGGTGAA GTGCTTGCAT GGATCTATAG AAATTACA

(SEQ ID NO 123)

Figure 49

CAAATGGAGT TTTTATTTT TATTATCTT AACACCCCAT TAAATTTTTC GGTGTTAAA CCCAAATCAA  
TGTTTGGTCT CACAACTAAC ACATTTGGTC AGTTGTATC CAGTCTGAA AGAATGTTTT TGAACAGTTC  
TTTCAAAAC T GAAAACGACA ATCTTCTAG TTCCAAAAT AAATACCAA GGATCAATAC AATAAGTTAC  
TAAGGGCTTA TGGT

(SEQ ID NO 124)

Figure 50

CTAATGAAGT TTTTACTTT TTCTTTTCAT CTTTAATAAA GATAAATACT AAACAAAACA TCAAAATCCA  
TTTATTATC GGTGGTAAAT TAAACCCAAA TCCCTGTTTG GTCTCACAAC TAACATATTT GGTGAGATTG  
TATCCAGTTC TGAAAGAACA TTTCCGCTTC TTTCAAAACT GAAAACGACA ATCTTCTAG TTCCAAATAA  
ATACCAAAGG ATCAATACAA TAAGTTACTA AGGCTTATG GT

(SEQ ID NO 125)

Figure 51

AACGAAAGAT TGACGATTGG TAAGAAATCCA CAACAAAGTTG TTCTTCATAG ATGTATCTGA GGGTCTGTAG  
CTCAGTTGGT TAGAGCACAC GCTTGATAAG CGTGGGGTCA CAAGTTC AAG TCTTGT CAGA CCCACCATGA  
CTTTGACTGG TTGAAGTTAT AGATAAAAGA TACATGATTG ATGATGTAAG CTGGGGACTT AGCTTAGTTG  
GTAGAGCGCC TGCTTTGCAC GCAGGAGGTC AGGAGTTCGA CTCCTCCTAGT CTCCACCAGA ACTTAAAGATA  
AGTTCGGATT ACAGAAATTA GTAAATAAAG ATTGAGATCT TGGTTTATTA ACTTCTGTGA TTTTCATTATC  
ACGGTAATT A GTGTGATCTG ACGAAGACAC ATTAAC TCA T TAACAGATTG GCAAAAT TGA GTCTGAAATA  
AATTGTTTCA C TCAAGAGTTT AGGTTAAGCA ATTAATCTAG ATGAATTGAG AACTAGCAAA TTAAC TGAAT  
CAAGCGTTTT GGTATGTGAA TTTAGATTGA AGCTGTACAG TGCTTAAAGTG CACAGTGCTC TAAACTGAAA  
TGTTGAAGTT ACTAACTTGT AGGTAACATC GACTGTTTGG GGTGTAT

(SEQ ID NO 126)

Figure 52

AACGAAAGAT TGACGATTGG TAAGAATCCA CGACAAGTTG TTCTTCATAG ATGTATCTGA GGGTCTGTAG  
CTCAGTTGGT TAGAGCACAC GCTTGATAAG CGTGGGGTCA CAAGTTCAAG TCTTGTCAGA CCCACCATGA  
CTTTGACTGG TTGAAGTTAT AGAAAAGAAG ATACATAACT GATGATGTAA GCTGGGGACT TAGCTTAGTT  
GGTAGAGCGC CTGCTTTGCA CGCAGGAGGT CAGGAGTTGG ACTCTCCTAG TCTCCACCA

(SEQ ID NO 127)

Figure 53

AACGAAAGAT TGATGGCCGG TAAGAATCCA CAACAAGTTG TTCTTCGAAG ATGTATCTGA GGGTCTGTAG  
CTCAGTTGGT TAGAGCACAC GCTTGATAAG CGTGGGGTCA CAAGTTCAAG TCTTGTGAGA CCCACCAAAT  
CTGAAAGATA TGTGTTTCAT TATGATTAAA GCTGGGGGACT TAGCTTAGTT GGTAGAGCGC CTGCTTTGCA  
CGCAGGAGGT CAGGAGTTTG ACTCTCCTAG TCTCCACCA

(SEQ ID NO 128)

Figure 54

AACGAAAGAT TGACGATTGG TAAGAATCCA CAACAAGTTG TTCTTCATGA CGATGTATCT GAGGGTCTGT  
AGCTCAGTTG GTTAGAGCAC ACGCTTGATA AGCGTGGGGT CACAAGTTCA AGTCTTGTCA GACCCACCAA  
ATCTGACTAA CAAGCATTAT TAAATGCTGA ATACAGAAAA ACAGAGACAT TGACTTATTG ATAAGCTGGG  
GACTTAGCTT AGTTGGTAGA GCGCCTGCTT TGCACGCAGG AGGTCAGGAG TTCGACTCTC CTAGTCTCCA  
CCA

(SEQ ID NO 129)

Figure 55

AACGAAAGAT TGGTGACCGG TAAGAATCCA CAACAAGTTG TTCTTCGAAG ATGTATCTGA GGGTCTGTAG  
CTCAGTTGGT TAGAGCACAC GCTTGATAAG CGTGGGGTCA CAAGTTCAAG TCTTGTCTAGA CCCACCACTA  
CTGACGAAGT GATGAATAAT CACAAGCTGC TAGATGAAAA GATATGTCGT TCATTATGAT TAAAGCTGGG  
GACTTAGCTT AGTTGGTAGA GCGCCTGCTT TGCACGCAGG AGGTCAGGAG TTCGACTCTC CTAGTCTCCA  
CCA

(SEQ ID NO 130)



Figure 56

TAAGGAAGAT CGAGAATTGG AAAGAGGTCG GATTATCCG GATGATCCTT CTCATCTTA TTAGAACATA  
 GATCGCAGGC CAGTCAGCCT GACGATCGCT TGCAGGCGTG CCGCCTTCGT TTCTCTTTCT TCAATTGTTGA  
 TTGCTCACGG GCCGTACCGC AGCTGACGCT GCTGGCCCTG CGCAGGCGCG GCCCATCAGG GCCGACGGCC  
 GGTCCGCCCTT GCNAAGCTTC GCTTCGGGGT GGATCTGTGG ATCGCGTAGT AGCGTTTGCG TCGGTATCTG  
 GGCTTGTAGC TCAGTTGGTT AGAGCACACG CTTGATAAGC GTGGGGTCGG AGTTCAAGT CCTCCCAGGC  
 CCACCAAGTT ACTTGATGAG GGGCCGTAGC TCAGCTGGGA GAGCACCTGC TTTGCAAGCA GGGGTCGTC  
 GGTTCGATCC CGTCCGGCTC CACCATCATG TTGGTGTTGA GACGGATATT GGCAATCAAC AAAAGAAAGA  
 AACAAAGTTG CGGACTNNTA CGAAAGTCTG CCTGTTCTGT ATGAAATCGT GAAGAGAAGA TGTAATCGGA  
 TCAACTGAAG AGTTGATGTC GCAAGAAGCT TGCTCAAGCC TTGCATAATG ATTGATGTGT TTAACCGCCA  
 TCACCGATTG TATCTCGAGA AGCTGGTCTT TCTGCTGATA CTGTTGAAAC GAGCATTTGC AGTCGAATGG  
 CAACATTCGG CGTCGCATAA TCGGGCTTTA AGAGCTGAGT TTTGATGGAT ATTGGCAATG AGAGTGATCA  
 AGTGTCTTAA GGGCATTGGT GGATGCCCTTG GCATGCAC

(SEQ ID NO 131)

Figure 57

TAAGGAGGAT CGAGAAATTGG AAAGAGGCCG GATTATCCG GATGATCCTT CTCCATCTTA TTAGAACATA  
 GATCGCAGNC CAGTCAGCCT GACGATCGCT TGCAGGCGTG CCGCCTTCGT TTCTCTTTCT TCATTGTTGA  
 TTGCTCACGG GCCGTACCGC AGCTGACGCT GCTGGCCCTG CGCAGGCGCG GNCCATCAGG GCCGACGGCC  
 GGTCGGCCTT GCGAAGCTTC GCTTCGGGT GGATCTGTGG ATCGCGTAGT AGCGTTTGG TCGGTATCTG  
 GGCTTGTAGC TCAGTTGGTT AGAGCACACG CTTGATAAGC GTGGGTCGG AGGTTCAAGT CCTCCCAGGC  
 CCACCAAGTT ACTTGATGAG GGGCCGTAGC TCAGCTGGGA GAGCACCTGC TTTGCAAGCA GGGGTCGTC  
 GGTTCGATCC CGTCCGGCTC CACCATCATG TTGGTGTTGA GACGGATATT GCCAATCAAC AAAAGAAAGA  
 AACAAAGTTG CGGACTNNTA CGAAAGTCTG CCTGTTCTGT ATGAAATCGT GAAGAGAAGA TGTAATCGGA  
 TCAACTGAAG AGTTGATGTC GCAAGAAGCT TGCTCAAGCC TTGCATAATG ATTGATGTGT TTAACCGCCA  
 TCACCGATTG TATCTCGAGA AGCTGGTCTT TCTGCTGATA CTGTTGAAAC GAGCATTTGC AGTCGAATGG  
 CAACATTCCG CGTCGCATAA TGCCGCCTTA AGAGCTGAGT TTTGATGGAT ATTGGCAATG AGAGTGATCA  
 AGTGTCTTAA GGGCATTTGGT GGATGCCCTTG GCATGCAC

(SEQ ID NO 132)

Figure 58

CCTTAAAGAA CTGTTCTTTG CAGTGCTCAC ACAGATTGTC TGATGAAAAG TAAATAGCAA GCGTCTTGC  
GAAGCAGACT GATACGTCCC CTTCGTCTAG AGGCCCAGGA CACCGCCCTT TCACGGCGGT AACAGGGTT  
CGAATCCCCT AGGGACGCC ACTTGC GCGG TAATGTGTGA AAGCGTTGCC ATCAGTATCT CAAAAC TGAC  
TTACGAGTCA CGTTTGAGAT ATTTGCTCTT TAAAAATCTG GATCAAGCTG AAAATTGAAA CACAGAACAA  
CGAAAGTTGT TCGTGAGTCT CTCAAATTTT CGCAACACGA TGATGAATCG TAAGAAACAT CTTCCGGGTTG  
TGA

(SEQ ID NO 133)

Figure 59

CCTTAAAGAA CTGTTCTTTG CAGTGCTCAC ACAGATTGTC TGATGAAAAA CGAGCAGTAA AACCTCTACA  
GGCTTGTAGC TCAGGTGGTT AGAGCGCACC CCTGATAAGG GTGAGGTCGG TGGTTCAAGT CCACTCAGGC  
CTACCAAATT TTCCCTGAAT ACTGCGTTGT GAAATAACTC ACATACTGAT GTATGCTTCG TTATTCCACG  
CCTTGTCTCA GGAAAAATTA TCGGTAAAGA GGTCTGACT ACACGATGGG GCTATAGCTC AGCTGGGAGA  
GCGCCTGCTT TGCACGCAGG AGGTCTGCGG TTCGATCCCG CATAGCTCCA CCATATCGTG AGTGTTTACG  
AAAAAATACT TCAGAGTGTA CCTGAAAGGG TTCACTGCCA AGTTTGTCTC TTTAAAAATC TGGATCAAGC  
TGAAAAATTGA AACACAGAAC AACGAAAGTT GTTCGTGAGT CTCTCAAATT TTCGCAACAC GATGATGAAT  
CGTAAGAAAC ATCTCGGGT TGTGA

(SEQ ID NO 134)

Figure 60

CCTTAAAGAA GCGTACTTTG CAGTGCTCAC ACAGATTGTC TGATGAAAAG TAAATAGCAA GCGTCTTGC  
GAAGCAGACT GATACGTCCC CTTCGTCTAG AGGCCCAGGA CACCGCCCTT TCACGGCGGT AACAGGGGT  
CGAATCCCT AGGGACGCC ACTTGC GCGG TAAATGTGTA AAGCGTTGCC ATCAGTATCT CAAAAC TGAC  
TTACGAGTCA CGTTTGAGAT ATTTGCTCTT TAAAAATCTG GATCAAGCTG AAAATTGAAA CACAGAACAA  
CGAAAGTTGT TCGTGAGTCT CTCAAATTTT CGCAACACGA TGATGAATCG TAAGAAACAT CTTCCGGGTTG  
TGA

(SEQ ID NO 135)

Figure 61

CCTTAAAGAA CTGTTCTTTG AAGTGCTCAC ACAGATTGTC TGATGAAAAA CGAGCAGTAA AACCTCTACA  
GGCTTGTAGC TCAGGTGGTT AGAGCGCACC CCTGATAAGG GTGAGGTCGG TGGTTCAAGT CCACTCAGGC  
CTACCAAATT TTCCCTGAAT ACTGCGTTGT GAAATAACTC ACATACTGAT GTATGCTTCG TTATTCCACG  
CCTTGTCTCA GGAAAAATTA TCGGTAAAGA GGTCTGACT ACACGATGGG GCTATAGCTC AGCTGGGAGA  
GCGCCTGCTT TGCACGCAGG AGGTCTGCGG TTCGATCCCG CATAGCTCCA CCATCTCGTG AGTGTTTACG  
AAAAAATACT TCAGAGTGTA CCTGAAAAGG TTCACCTGCCA AGTTTGTGCTC TTTAAAAATC TGGATCAAGC  
TGAAAAATTGA AACACAGAAC AACGAAAAGTT GTTCGTGAGT CTCCTCAAATT TTCGCAACAC G

(SEQ ID NO 136)

Figure 62

CCTTAAAGAA GCGTACTTTG AAGTGCTCAC ACAGATTGTC TGATGAAAAG TGAATAGCAA GCGTCTTGC  
GATTGAGACT TCAGTGTCCC CTTCGTCTAG AGGCCCAGGA CACCGCCCTT TCACGGCGGT AACAGGGTT  
CGAATCCCCT AGGGGACGCC AGCGTTCAAA CTGATGAGGT CAAACCTCCA GGGACGCCAC TTGCTGGTTT  
GTGAGTGAAA GTCACCTGCC TTAATATCTC AAAACTGACT TACGAGTCAC GTTTGAGATA TTTGCTCTTT  
AAAAATCTGG ATCAAGCTGA AAATTGAAAC ACAGAACAAC GAAAGTTGTT CGTGAGTCTC TCAAAATTTTC  
GCAACACGAT GATGAATCGT AAGAAACATC TTCGGGTTGT GA

(SEQ ID NO 137)

Figure 63

CCTTAAAGAA ACGGTCTTTG AAGTGCTCAC ACAGATTGTC TGATGAAAAA CGAGCAGTAA AACCTCTACA  
GGCTTGTAGC TCAGGTGGTT AGAGCGCACC CCTGATAAGG GTGAGGTCGG TGGTTCAAGT CCACTCAGGC  
CTACCAAATT TTCCCTGAAT ACTGCCGTTGT GAAATAACTC ACATACTGAT GTATGCTTCG TTATTCCACG  
CCTTGCTCA GGAAAAATTA TCGGTAAAGA GGTTCCTGACT ACACGATGGG GCTATAGCTC AGCTGGGAGA  
GCGCCTGCTT TGCACGCAGG AGGCTGCGG TTCGATCCCG CATAGCTCCA CCATCTCGTG AGTGTTTACG  
AAAAAATACT TCAGAGTGTA CCTGAAAGGG TTCACTGCCA AGTTTGTCTC TTTAAAAATC TGGATCAAGC  
TGAAAAATTGA AACACAGAAC AACGAAAGTT GTTCGTGAGT CTCTCAAATT TTCGCAACAC GATGATGAAT  
CGTAAGAAAC ATCTTCGGGT TGTGA

(SEQ ID NO 138)



Figure 64

CTAAGGATAT ATTGGAACA TCTTCTTCGG AAGATGCCGA ATAACGTGAC ATATTGTATT CAGTTTGGAA  
TGTTTATTTA ACATTCAAAT ATTTTGTGGT TAAAGTGATA TTGCTTTTGA AAATAAAGCA GTATGCGAGC  
GCTTGACTAA AAAAAATTGT ACATTGAAAA CTAGATAAGT AAGTAAAAATA TAGATTTTAC CAAGCAAAAC  
CGAGTGAATA AAGAGTTTTA AATAAGCTTG AATTCATAAG AAATAATCGC TAGTGTTTCA AAGAACAACCTC  
ACAAAGATTAA TAACGCGTTT AAATCTTTT ATAAAAGAAC GTAACTTCAT GTTAAACGTTT GACTTATAAA  
AATGGTGGAA ACATA

(SEQ ID NO 139)

Figure 65

CTAAGGATAT ATTCGGAACA TCTTCTTCAG AAGATGCGGA ATAAACGTGAC ATATTGTATT CAGTTTGGAA  
TGTTTATTTA ACATTCAAAT ATTTTITGGT TAAAGTGATA TTGCTTATGC GAGCNCCTTGA CAATCTATTC  
TTTTTTAAAGA AAGCGGTTGT CAGACAATGC ATTAAGAAAA ATTAAAGCGG AGTTTACTTT TGTAAATGAG  
CATTGATTT TTTGAAAATA AAGCAGTATG CGAGCGCTTG ACTAAAAAGA AATTGTACAT TGA AAAACTAG  
ATAAGTAAGT AAAATATAGA TTTTACCAAG CAAAACCGAG TGAATAAAGA GTTTTAAATA AGCTTGAATT  
CATAAGAAAT AATCGCTAGT GTTCGAAAGA ACACTCACAA GATTAATAAC GCGTTTAAAT CTTTTATATA  
AAGAAAAACGT TTAGCAGACA ATGAGTTAAA TTATTTTAAA GCAGAGTTTA CTTATGTAAA TGAGCATTTA  
AAATAATGAA AACGAAGCCG TATGTGAGCA TTTGACTTAT AAAAATGGTG GAAACATA

(SEQ ID NO 140)

Figure 66

CTAAGGATAT ATTCGGAACA TCTTCTTCAG AAGATGCGGA ATAACGTGAC ATATTGTATT CAGTTTGGAA  
TGTTTATTTA ACATTCAAAT ATTTTGTGGT TAAAGTGATA TTGCTTATGC GAGCGCTTGA CAATCTATTC  
TTTTTAAAGA AAGCGGTTGT CAGACAATGC ATTAAGAAAA ATTAAAGCCG AGTTTACTTT TGTAAATGAG  
CATTGTATTT TTTGAAAATA AAGCAGTATG CGAGCGCTTG ACTAAAANGA AATTGTACAT TGAAAACTAG  
ATAAGTAAAGT AAAATATAGA TTTTACCAAG CAAAACCGAG TGAATAAAGA GTTTTGAATA AGCTTGAATT  
CATAAGAAAT AATCGCTAGT GTTCGAAAGA ACACTCACAA GATTATAAC GCGTTTAAAT CTTTTTATAA  
AAGAACGTAA CTTCATGTTA ACGTTTGAAT TATAAAAATG GTGGAAACAT A

(SEQ ID NO 141)

Figure 67

CTAAGGATAT ATTGGGAACA TCTTCTTCAG AAGATGCGGA ATAACGTGAC ATATTGTATT CAGNTTTGAA  
TGTTTATTTA ACATTCAAAA AATGGGCCCTA TAGCTCAGCT GGTAGAGCG CACGCCCTGAT AAGCGTGAGG  
TCGGTGGTTC GAGTCCACTT AGGCCCCACCA TTATTTGTAC ATTGAAAACT AGATAAGTAA GTAAAAATATA  
GATTTTACCA AGCAAAACCG AGTGAATAAA GAGTTTTAAA TAAGCTTGAA TTCATAAGAA ATAATCGCTA  
GTGTTTCGAAA GAACACTCAC AAGATTAATA ACGCGTTTAA ATCTTTTAT AAAAGAACGT AACTTCATGT  
TAACGTTTGA CTTATAAAAA TGGTGGAAC ATA

(SEQ ID NO 142)

Figure 68

CTAAGGATAT ATTCGGAACA TCTTCYTCAG AAGATGCCGA ATAATGTGAC ATATTGTATT CAGTTTGTGAA  
TGTTTATTTA ACATTCAAAT ATTTTGTGGT TAAAGTGATA TTGCTTATGC GAGCGCTTGA CTAAAAAGAA  
ATTGTACATT GAAAACTAGA TAAGTAAAGTA AAANTATAGA TTTTACCAAG CAAAACCGAG TGAATAAAGA  
GTTTAAATA AGCTTGAATT CATAAGAAAT AATCGCTAGT GTTCGAAAAGA AACTCACAA GATTAATAAC  
GCGTTTAAAT CTTTTTATAA AAGAACGTAA CTTTCATGTTA ACGTTTGACT TATAAAAATG GTGAAAACAT

A

(SEQ ID NO 143)

Figure 69

CTAAGGATAT ATTGGAACA TCTTCTACGA AGATGAGGGA ATAACGTGAC ATATTGTATT CAGTTTGGAA  
TGTTTATTAA CATTCAATTG TACATTGAAA ACTAGATAAG TAAGTAAGAT TTTACCAAGC AAAACCGAGT  
GAATAGAGTT TTAATAAGC TTGAATTTCAT AAATAATCGC TAGTGTTCCG AAGACNTCCA CAAGATTAAAT  
AACTAGTTTT AGCTATTTAT TTTGAATAAC AATTCAAAAT ATGGTGGGAC ATA

(SEQ ID NO 144)

Figure 70

AAGGATAAGG AACTGCACAT TGGTCTTGTT TAGTCTTGAG AGGTCTTGTG GGGCCTTAGC TCAGCTGGGA  
GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTTTCGATCC CGCTAGGCTC CATTGGTGAG AGATCACCAA  
GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA ACAAGAAAAT AAACCGAAAA CGCTGTAGTA  
TTAATAAAGA GTTTATGACT GAAAGGTCAA AAAATAA

(SEQ ID NO 145)

Figure 71

AAGGAAATGG AACACGTTTA TCGTCTTATT TAGTTTGTAG AGGTCTTGTG GGGCCTTAGC TCAGCTGGGA  
GAGCGCTGC TTNGCACGCA GGAGGTCAGC GGTCGATCC CGCTAGGCTC CATCAGGATA CANTCCTACT  
AAACTTAATA CAAGTGAAGT TGAACACGCA ACTCACTTCC TAGGAAAATA GACAATCTTC GCTTGTGTGC  
AAGGCACACA TGGTCAGATT CCTAATTTC TACAGAAAGT TCGCTAAAAGC GAGCGTTGCT TAGTATCCTA  
TATAATAGTC CATNGAAAAT TGAATATCTA TATCAAAATTC CACGATCTAG AAATAGATTG TGGAAAACGTA  
ACAAGAAATT AACCCGNAAA CGCTG

(SEQ ID NO 146)



Figure 72

AAGGATAAGG AACTGCACAT TGGTCTTGTT TAGTCTTGAG AGGTCTTGTC GGGCCTTAGC TCAGCTGGGA  
GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTCGATCC CGCTAGGCTC CATTTGGTGAG AGATCACCAA  
GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA ACAAGAAAAT AAACCGAAAC GCTGTAGTAT  
TAAAAGAGTT TATGACTGAA AGGTCAGAAA ATAA

(SEQ ID NO 147)

Figure 73

CTAAGGATAT ATTCGGAACA TCCTCTTACG AAGATGCAGG AATAACATTG ACATATTGTA TTCAGNTGTG  
AATGCTCATT GGAGNATTCA TNGCATNATT TGGTNCATTG ACANCTAGAT AAGNAAGTAA AATTATGAT  
TTTACCAAGC AAAACCGAGT GAATTAGAGT TNTNNAACAA GCCTTGATTT CAAAAAGAAA TAATCGCTAG  
TGTTTCGAAAG AACACTCACA GATTANTAAC ATCTTGGGTT TTCACCCGAC TTGTTCTGTT CGAAAGTCAA  
AAA

(SEQ ID NO 148)

Figure 74

AAGGATAAGG AACTGCGCAT TGGTCTTGTT TAGTCTTGAG AGGTCTTGTG GGGCCTTAGC TCAGCTGGGA  
GAGCGCCTGC TTTGCAACGCA GGAGGTCAGC GGTTCCGATCC CGCTAGGCTC CATTGGTGAG AGATCACCAA  
GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA ACAAGAAAAT AAACCGAAAA CGCTGTAGTA  
TTAATAAGAG TTTATGACTG AAAGGTCAAA AAATAA

(SEQ ID NO 149)

Figure 75

AAGGATAAGG AACTGCCGCAT TGGTCTTGTT TAGTCTTGAG AGTCTTGTG GGGCCTTAGC TCAGCTGGGA  
GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTTCGATCC CGCTAGGCTC CATTGGTGAG AGATCACCAA  
GTAATGCACA TTGAAAAATTG AATATCTATA TCAATAGTA ACAAGAAAAT AAACCGAAAA CGCTGTAGTA  
TTAATAAGAG TTTATGACTG AAAGGTCAGA AAAATAA

(SEQ ID NO 150)

Figure 76

AAGGAAAAGG AACTGCGCAT TGGTCTTGTT TAGTCTTGAG AGGTCTTGTT GGCCTTAGC TCAGCTGGGA  
GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTCGATCC CGCTAGGCTC CATGGTGAG AGATCACCAA  
GTAATGCCACA TTGAAAATTG AATATCTATA TCAAATAGTA ACAAGAAAT AAACCGAAAA CGCTGTAGTA  
TTAATAAGAG TTTATGACTG AAAGGTCAGA AAAATAA

(SEQ ID NO 151)

Figure 77

AAGGATAAGG AACTGCGCAT TGGTCTTGTT TAGTCTTGAG AGGTCTTGTG GGGCCTTAGC TCAGCTGGGA  
GAGCGCCTGC TTGACACGCA GGAGGTCAGC GGTCGATCC CGCTAGGCTC CATGGTGAG AGATCACCAA  
GTAATGCACA TTGAAAATTG AATATCTATA TCAAAATAGTA ACAAGAAAAT AAACCGAAAC GCTGTAGTAT  
TAAAGAGTT TATGACTGAA AGGTCAGAAA ATAA

(SEQ ID NO 152)

Figure 78

AAGGATAAGG AACTGCGCAT TGGTCTTGTT TAGTCTTGAG AGGTCTTGTG GGGCCTTAGC TCAGCTGGGA  
GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTTGATCC CGCTAGGCTC CATTGGTGAG AGATCACCAA  
GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA ACAAGAAAAT AAACCGAAAC GCTGTAGTAT  
TAAAAGAGTT TATGACTGAA AGGTCAAAA TAA

(SEQ ID NO 153)

Figure 79

TAAGGAAGAT CGAGAATTGG AAAGAGGTCG GATTATCCG GATGATCCTT CTCCATCTTA TTAGAACATA  
 GATCGCAGG CAGTCAGCCT GACGATCGCT TGCAGGCGTG CCGCCTTCGT TTCTCTTTCT TCATTGTTGA  
 TTGCTCACGG GCCGTACCGC AGCTGACGCT GCTGGCCCTG CGCAGGCGCG GCCCATCAGG GCCGAACGGC  
 CGGTCGGCCT TGCNAAAGCTT CGCTTCGGGG TGGATCTGTG GATCGCGTAG TAGCGTTTGC GTCGGTATCT  
 GGGCTTGTA GCTCAGTTGGT TAGAGCACAC GCTTGATAAG CGTGGGGTCG GAGGTTCAAG TCCTCCCAGG  
 CCCACCAAGT TACTTGATGA GGGCCCGTAG CTCAGCTGGG AGAGCACCTG CTTTGCAAGC AGGGGTCGT  
 CGGTTCGATC CCGTCCGGCT CCACCATCAT GTTGGTGTG AGACGGATAT TGGCAATCAA CAAAAGAAAG  
 AAACAAAGTT GCGGACTNNT ACGAAAGTCT GCCTGTTCTG TATGAAATCG TGAAGAGAAG ATGTAATCGG  
 ATCAACTGAA GAGTTGATGT CGCAAGAAGC TTGCTCAAGC CTTGCATAAT GATTGATGT TTAAACCGCC  
 ATCACCATT GTATCTCGAG AAGCTGGTCT TTCTGCTGAT ACTGTTGAAA CGAGCATTTG CAGTCGAATG  
 GCAACATTG CCGTCGCATA ATGCGGCTTT AAGAGCTGAG TTTTGATGGA TATTGGCAAT GAGAGTGATC  
 AAGTGTCTTA AGGCAATTG TGGATGCCCTT GGCATGCAC

(SEQ ID NO 154)



Figure 80

AAGGAGCACC ACGAGAAACA CTCCAATTGG TGGGGTGTA A GCGGTGAGGG GTTCTCGTCT GTAGTGGACG  
GAAGCCGGGT GCACAACAAC AAGCAAGCCA GACACACTAT TGGGTCCCTGA GGCAACATCT CTGTTGGTTT  
CGGGATGTTG TCCCACCATC TTGGTGGTGG GGTGTGGTGT TTAGAATTTG GATAGTGGTT GCGAGCATCA  
ATTGGATGCG CTGCCCTTTG GTGGCGTGT CTGTTGTGCA ATTTATTCT TTGGTTTTG TGTATTAT

(SEQ ID NO 157)

Figure 81

AAGGAGCACC ACGAGAAACA CCCCAATTGG TGGGGTGTGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
AGGGCCGGGT GCACAACAAC AGGCAATCGC CGGACACACT ATTGGGCCCT GAGACAACAC TCGGCCGACT  
GAGGTCGACG TGGTGTCCCT CCATCTTGGT GGTGGGGTGT GGTGTTTGAG CATTGAATAG TGGTTGCGAG  
CATCTAGCCG GATGCGTTCC CCAGTGGTGC GCGTTCGTCA AAAATGTGTA ATTTTCTTTT TGGTTTITGT  
GTTCGT

(SEQ ID NO 158)

Figure 82

AAGGAGCACC ACGAGAAACA CCCCAATTGG TGGGGTGTGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
AGGGCCGGGT GCACAACAAC AGGCAATCGC CGGACACACT ATTGGGCCCT GAGACAACAC TCGGCCGACT  
GAGGTCGACG TGGTGTCCCT CCATCTTGGT GGTGGGGTGT GGTGTTTGAG CATGAATAG TGGTTCCGAG  
CATCTAGACG GATGCGTTCC CCAGTGTGC GCGTTCGTCA AAAATGTGTA ATTTTCTTT TGGTTTGTGT  
GTTCGT

(SEQ ID NO 159)

Figure 83

AAGGAGCACC ACGAGAAACA CCCCAATTGG TGGGGTGTGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
AGGNNCGGGT NNACAAACAAC NGCCAATCGC CGGACACACT ATTGGGNCCT GAGACAACAC TCGGCCGACT  
GAGGTCGACG TGGTGTCCTT CCATCTTGGT GGTGGGGTGT GGTGTTGAG CATGAATAG TGGTTGCCGAG  
CATCTAGCCG GATGCGTTCC CCAGTGGTGC GCGTTCGTCA AAAATGTGTA ATTTTCTNT TGGTTTTTGT  
GTTTCGT

(SEQ ID NO 160)

Figure 84

AAGGAGCAC ACCAGAAACA CTCCAATTGG TGGAGTGTGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
AGGGCCGGGT GCACAACAGC AGACAATCGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGCCGACT  
TTGGTCGACG TGGTGTCCCT CCATCTTGGT GGTGGGGTGT GGTGTTTGAG CATTGAATAG TGGTTGCCGAG  
CATCTAGACG GATGCGTTGC CCTCGGGCCG CGTGTTCGTC AAAAATGTGT AATTTTCT TTTGGTTTTT  
GTGTTCTGT

(SEQ ID NO 161)

Figure 85

AAGGAGCACC ACGAGAAACA CTCCAATTGG TGGAGTGTGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
GGAGCCCGGT GCACAACAAC AGGCAATCGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGCCGGCT  
TTGAGTCGAA GTGGTGTCCC TCCATCTTGG TGGTGGGGTG TGGTGTTTGA GCATTGAATA GTGGTTGCCA  
GCATCTAGAC GGATGCCGTTG CCTTCGGGCC GCGTGTTCGT CAAAAATGTG TAATTTTTC TTTTGGTTTT  
TGTGTTTCGT

(SEQ ID NO 162)

Figure 86

AGGAGCACC GNAACGCAT CCCGCGTGGG GTGTGGGTTT GCGGTGTTGT GCGTCGGNC CGAGGTGTTG  
GGCAGCAGGC AGTAACCNCC GGAACACTGT TGGGTTTGA GNNAAACACC GTGGTGGTGT TGTGCTCCCC  
GTGGTGNCGG GGTGTGGTGT TTGAGTGTTG GATAGTGGTT GCGAGCATCT GGCAAGACT GTGGTAAGCG  
GTTTTTGTTG ANTGTTTCT GGTGTTTGT

(SEQ ID NO 163)

Figure 87

AAGGAGCACC ACGAGAAACA CTCCAATTGG TGGGGTGTGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
AGGNCGGGT GCACAACAAC AGNCAATCGC CAGACACACT ATTGGNCCCT GAGACAACAC TCGGCCGACT  
TNGGTTGAAG TGGTGTCCCT CCATCTTGGT GGTGGGGTGT GGTGTTTGAG TATTGATAG TGGTTGCCGAG  
CATCTAANTG AACGCGTCGC CGNCAACGGT TACGTGTTCC TTTTGTGTAA TTNNTTCTAT TGGTTTTTGT  
GTTCGT

(SEQ ID NO 164)



Figure 88

AAGGAGCACC ACGAGAAACA CTCCAATTGG TGGGGTGTGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
AGGGCCGGGT GCACAACAAC AGGCAATCGC CAGACACACT ATTGNNCCCT GAGACAACAC TCGGCCGACT  
TTGGTCGAAG TGGTGTCCCC CCATCTTGGT GGTGGGGTGT GGTGTTTCAG TATTGGATAG TGGTTGCGAA  
CATCTAAATG AACGCGTTGC CGGCAACGGT TACGTGTTTCG TTTTAGTGTA ATTNTTCTA ATGGTTTTTG  
TGTTTCGT

(SEQ ID NO 165)

Figure 89

AAGGAGCACC ACGAGACCTG GGCCGGCCCC GCAGATCGCG GGATCAGCTG AGCTTTCAGG CGATTCGTTG  
GATGGCCTCG CACCTGTAGT GGGTGGGGT CTGGTGCACT CAACAACCTT GGCGTGGGAT GCGGGAAGC  
ATCTGCCGGA AATCATCAGA CACACTATTG GGCTTTGAGA CAACAGGCC GCAGNCCTGN CCCGTTGGGG  
GCAGNGGGTG TGTGTGGCC TCACTTTGGT GGTGGGGTG GTGTTGATT TGTGGATAGT GGTTCGAGC  
ATCTAGCGCG CAGAAATGTGT GGTCTCACTC CTTGTGGGTG GGGCCTGGTT TTGTGTGCGA TTGATGTGCA  
ATTCTTTTG AAACATCATTT TTTGGTTTTT GTGTTGT

(SEQ ID NO 166)

Figure 90

AAGGAGCACC ACGAAAAACT CCCCAATTGG TGGGGTGTA A GCCGTGAGGG GTTCCCGTCT GTAGTGGACG  
GGGGCCGGGT GCGCAACAGC AAGCGAAACG CCGGACACAC TATTGGGTCC TGAGGCAACA CTCGGGTTTG  
TCCCCCTCAG GGATTTTCTG GGTGTTGTCC CACCATCTTG GTGGTGGGGT GTGGTGTG AGAATTGGAT  
AGTGGTTGCG AGCATCAAAT GGATGCGTTG CCCCTACGGG TAGCGTGTC TTTTGTGCAA TTTTATTCNT  
TGGTTTTTGT GTTTGT

(SEQ ID NO 167)

Figure 91

AAGGAGCACC ACGAGAAAGCA CTCCAACTGG TGGGGTGCAA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG  
AGAGCCCGGT GCGCGACAAC GAACGAGCCA GACACACTAT TGGGTCCCTGA GGCAACACTC GGGCTTGGCC  
AGAGCTGTG TCCCACCATC TTGGTGGTGG GGTGTGGTGT TTGAGAATTG GATAGTGGTT GCGAGCATCA  
AATGGATGCG TTGCCCCCTAC GGGTGGCGTG TTCTTTTG TG CAATTTTAT CTTTGGTTTT TGTGTTGT

(SEQ ID NO 168)

Figure 92

AAGGAGCACC ACGAAAAACA CCCCAACTGG TGGGGTGTA A GCCGTGAGGG GCTCCCGTCT GTAGTAGACG  
GGCGCCGGGT GCGCAACAGC AAGCGAGCCA GACACACTAT TGGGTCCCTGA GGCAACACTC GGGCTTGTCT  
TGGACTCGTC CAAGAGTGTT GTCCCAACCAT CTTGGTGGTG GGGTGTGGTG TTTGAGAATT GGATAGTGGT  
TGCAGCATC ANCTGGATGC GTTGCCCCCA GGGGTAGCGT GTTCTTTTGT GCAATTNTAT TCNNTGGTTT  
TTGTGTTAGT

(SEQ ID NO 169)

Figure 93

AAGGAGCACC ACGAAAAACA CTCGCGCATCC GGTGGGGTGT GAGCCGTGAG GGAGCCCGTG CCTGTAGTGG  
GTGTGGGTG GGTGCGCGAC AACAAATGGG AAAAATCGCT GGGCACACTA TTGGGCTTTG AGGCAACACC  
TGGTTTGT TTGGGTGGTGT CGCTCCATCT TGGTGGTGG GTGTGGTGT TGAGTTGTGG ATAGTGGTTG  
CGAGCATCTA AGCAAAAGCT GTTGTGTGAC GGTTTTGTG GAGTGTGTG TGTGT

(SEQ ID NO 170)

Figure 94

AAGGAGCACC ACGAAAAACA CTCCAATTGG TGGGGTGTA A GCCGTGAGGG GTTCTCATCT GTAGTGGACG  
AGAGCCCGGT GCACAAACAGC AATGAATCG CCAGACACAC TGTGGGTCC TGAGGCAACA CTCAGGCTTG  
TCCCATGTTG GGCTTGATCG GGTGCTGTCC CCCCATCTTG GTGGTGGGT GTGGTGTG AGTATTGGAT  
AGTGGTTGCG AGCATCTAAA TGGATACGTT GCCAGTAATG GTGGCGTATT CATGAAAAT GTGTAATTT  
CTTCTTTGGT TTTGTGTGT

(SEQ ID NO 171)

Figure 95

AAGGAGCACC ACGAAAAACA CTCCAATTGG TGGGGTGTAAG GCCGTGAGGG GTTCTCATCT GTAGTGGACG  
AGAGCCGGGT GCACAACAGC AAATGAATCG CCAGACACAC TGTGGGTCC TGAGGCAACA CTCAGGCTTG  
TCCCATGTTG GGCTTGATCG GGTGCTGTCC CCCATCTTG GTGGTGGGT GTGGTGTG AGTATTGGAT  
AGTGGTTGCG AGCATCTAAA TGGATACGTT GCCAGTAATG GTGGCGTGTT CATTGAAAAT GTGTAATTTT  
CTTCTTTGGT TTTGTGTGT

(SEQ ID NO 172)



Figure 96

AAGGAGCACC ACGAAAAACA CTCCAATTGG TGGGGTGTA A GCCGTGAGGG GTTCTCATCT GTAGTGGACG  
AGAGCCCGGT GCACAACAGC AATGAATCG CCAGACACAC TGTGGGTCC TGAGGCAACA CTCAGGCTTG  
TCCCATGTTG GGCTTGATCG GGTGCTGTCC CCCCATCTTG GTGGTGGGGT GTGGTGTGTTG AGTATTGGAT  
AGTGGTTGCG AGCATCTAAA TGGANACGTT GCCAGTAATG GTGGCGTGTT CATTGAAAAT GTGTAATTTT  
CTTCTTTGGT TTTGTGTGT

(SEQ ID NO 173)

Figure 97

AAGGAGCACC ATTTCTCAGT CGAATGAACT GAGAACATAA AGCGAGTATC TGTA GTGGAT ACATGCTTGG  
TGAATATGTT TTATAAATCC TGTCCACCCC GTGGATAGGT AGTCGGCAAA ACGTCGGACT GTCATAAGAA  
TTGAAACGCT GGCACACTGT TGGGTCCTGA GGCAACACAT TGTGTTGTCA CCTGCTTGG TGGTGGGGTG  
TGGTCCTTGA CTTATGGATA GTGGTTGCCA GCATCTAAAC ATAGCCTCGC TCGTTTTCGA GTGAGGCTGG  
TTTTTGCAAT TTTATTAGCT

(SEQ ID NO 174)

Figure 98

CCTAATGATA TTGATTGCGG TGAAGTGCTC ACACAGATTG TCTGATGAAA AAGTAACGAG CAGAAATACC  
TTTATAGGCT TGTAGCTCAG GTGGTTAGAG CGCACCCCTG ATAAGGGTGA GGTCGGTGGT TCAAGTCCAC  
TCAGGCCTAC CACTTCTCGA AGTGGAAAAG GTACTGCACG TGA CTGTATG GGGCTATAGC TCAGCTGGGA  
GAGCGCCTGC CTTGCACGCA GGAGGTCAGC GGTTGATCC CGCTTAGCTC CACCATAATAG TCCTGTATTT  
CAATACTTCA GAGTGTACTG GCAACAGTAT GCTGCGAAGT ATTTTGCTCT TTAACAATCT GGAACAAGCT  
GAAAATTGAA ACATGACAGC TGAAACTTAT CCTCCGCTAG AAGTATTGGG GTAAGGATTA ACCTGTCTATA  
GAGTCTCTCA AATGTAGCAG CACGAAAGTG GAAACACCTT CGGGTTGTGA

(SEQ ID NO 195)

Figure 99

CCTAATGATA TTGATTGCG TGAAGTGCTC ACACAGATTG TTTGATAGAA ACGTAATGAG CAAAAGCGCT  
ACCTGTTGAT GTAATGAGTC ACTGACTCAT GCTGATACGA ACCGATTAAAG ACAGTCAGTT TAATCGGATT  
TTCGTGTCCC CATCGTCTAG AGGCCTAGGA CACTGCCCTT TCACGGCTGT AACAGGGTT CGAATCCCCT  
TGGGGACGCC ATTCGATAAT GAGTGAAAGA CATTATCACC GGTTCTTGA ACCGAAAAACA TCTTAAAGAT  
GACTCTTGCG AGTCGTGTTT AAGATATTGC TCTTTAAACA TCTGGAACAA GCTGAAAAATT GAAACATGAC  
AGCTGAAACT TATCCCTCCG TAGAAGTATT GGGGTAAGGA TTAACCTGTC ATAGAGTCTC TCAAATGTAG  
CAGCACGAAA GTGGAACAC CTTCGGGTTG TGA

(SEQ ID NO 196)

Figure 100

TAAGGATAAG GAAGAAGCCT GAGAAGGTTT CTGACTAGGT TGGGCAAGCA TTTATATGTA AGAGCAAGCA  
TTCTATTCA TTTGTGTTGT TAAGAGTAGC GCGGTGAGGA CGAGACATAT AGTTGTGAT CAAGTATGTT  
ATTGTAAGA AATAATCATG GTAACAAGTA TATTCACGC ATAATAATAG ACGTTTAAGA GTATTGTCT  
TTAGGTGAA GTGCTTGCAT GGATCTATAG AAATTACA

(SEQ ID NO 197)

Figure 101

TAAGGATAAG GAAACCTGTG AATCTTTTC CCTTCTTTTG TTCAGTTTTG AGAGGTTTCAT CTCTCAAAAC  
GTGTTCTTTG AAAACTAGAT AAGAAAAGTT AGTGTAAGAA GACGAAGAGA AACCGTAGGT TTTTCTTCAA  
CCAAAACCGA GAATCAAACC GAGAAAGAAT CTTTCCGTTT TCATAAGCGA TCGCACGTTT ATGAAAACAC  
AACAAACACCT TCGTAAGAAG GATGA

(SEQ ID NO 213)

Figure 102

TAAGGATAAG GAAACCTGTG AATCTTTTTC CCTTCTTTTG TTCAGTTTGT AGAGGTCAAT GACGCTCATA  
CTGAGTACCA GGTGACACGT TTTTGAGGTG TCTCTTCGTA TGAGGGGCCT ATAGCTCAGC TGGTTAGAGC  
GCACGCCCTGA TAAGCGTGAG GTCGGTGGTT CGAGTCCACT TAGGCCCACT TTTTGTGAATA AACCTTTCTT  
TTTATATATGT TAATAAGGGG CCTTAGCTCA GCTGGGAGAG CGCCTGCTTT GCACGCAGGA GGTGAGCGGT  
TCGATCCCGC TAGGCTCCAC CAAAGATAGT TTGTTCTTTG AAAACTAGAT AAGAAAAAGTT AGTGTAATAA  
GACGAAAGAGA AACCGTAGGT TTTTCTTCAA CCAAAACCGA GAATCAAACC GAGAAAGAAT CTTTCCGTTT  
TCATAAGCGA TCGCACGTTT ATGAAAACAC AACAAACCT TCGTAAGAAG GATGA

(SEQ ID NO 214)

Figure 103

TAAGGATAAG GAAACCTGTG AATCTTTTTC CCTTCTTTTG TTCAGTTTIG AGAGGTCAAT GACGCTCATA  
CTGAGTACCA GGTGACACGT TTTTGAGGTG TCTCTTCGTA TGAGGGCCT ATAGCTCAGC TGGTTAGAGC  
GCACGCCCTGA TAAGCGTGAG GTCGGTGGTT CGAGTCCACT TAGGCCCACT TTTTGAATA AACCTTCTT  
TTTTATATGT TAATAAGGG CCTTAGCTCA GCTGGGAGAG CGCCTGCTTT GCACGCAGGA GGTGAGCGGT  
TCGATCCCGC TAGGCTCCAC CAAAGATAGT TTGTTCTTTG AAAACTAGAT AAGAAAAGTT AGTGTAATAA  
GACGAAGAGA AACCGTAGGT TTTTCTTCAA CCAAAACCGA GAAAGAATCT TTCCGTTTTC ATAAGCGATC  
GCACGTTTAT GAAACACAA CAACACCTTC GTAAGAAGGA TGA

(SEQ ID NO 215)



(19)



Europäisches Patentamt

European Patent Office

Office européen des brevets



(11)

**EP 1 088 899 A3**

(12)

**EUROPEAN PATENT APPLICATION**

(88) Date of publication A3:  
02.05.2001 Bulletin 2001/18

(51) Int Cl.7: **C12Q 1/68**

(43) Date of publication A2:  
04.04.2001 Bulletin 2001/14

(21) Application number: **01200037.8**

(22) Date of filing: **23.06.1995**

(84) Designated Contracting States:  
**AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL  
PT SE**  
Designated Extension States:  
**LT LV SI**

(30) Priority: **24.06.1994 EP 94870106**  
**07.04.1995 EP 95870032**

(62) Document number(s) of the earlier application(s) in  
accordance with Art. 76 EPC:  
**95924923.6 / 0 769 068**

(71) Applicant: **N.V. INNOGENETICS S.A.**  
**9052 Gent (BE)**

(72) Inventors:  
• **Jannes, Geert**  
**3010 Kessel-Lo (BE)**  
• **Rossau, Rudi**  
**2180 Ekeren (BE)**  
• **Van Heuverswyn, Hugo**  
**9270 Kalken (BE)**

(54) **Simultaneous detection, identification and differentiation of Eubacterial taxa using a hybridization assay**

(57) The present invention relates to a method for detection and identification of at least one micro-organism, or for the simultaneous detection of several micro-organisms in a sample, comprising the steps of:

- (i) if need be releasing, isolating or concentrating the polynucleic acids present in the sample;
- (ii) if need be amplifying the 16S-23S rRNA spacer region, or a part of it, with at least one suitable primer pair;
- (iii) hybridizing the polynucleic acids of step (i) or (ii) with at least one and preferably more than one of the spacer probes as mentioned in table Ia or equivalents of thereof, under the appropriate hybridization

and wash conditions, and/or with a taxon-specific probe derived from any of the spacer sequences as represented in figs. 1-103 under the same hybridization and wash conditions;

- (iv) detecting the hybrids formed in step (iii) with each of the probes used under appropriate hybridization and wash conditions;
- (v) identification of the micro-organism(s) present in the sample from the differential hybridization signals obtained in step (iv).

**EP 1 088 899 A3**



European Patent  
Office

# EUROPEAN SEARCH REPORT

Application Number  
EP 01 20 0037

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (InCL.7)
Y	WO 93 11264 A (DU PONT) 10 June 1993 (1993-06-10) * page 9, line 1 - line 4; figures 1,4 *	1	C12Q1/68
A	* page 11, line 18 - page 12, line 3 * * page 21, line 26 - page 23, line 4; example 3 *	2-10	
Y	--- T.M. SCHMIDT: METHODS IN MOLECULAR AND CELLULAR BIOLOGY, vol. 5, no. 1, 1994, pages 3-12, XP002160264 NEW YORK US * the whole document, especially tabe 1 *	1	
A	--- WO 93 04201 A (AMOCO CORPORATION) 4 March 1993 (1993-03-04) * page 19, line 12 - line 15 *	1,4-6	
A	--- J.W. VAN DER GIESSEN ET AL.: MICROBIOLOGY, vol. 140, no. 5, 1994, pages 1103-1108, XP002160258 READING GB * the whole document *	1,4-6	
A	--- Y. JI ET AL: MICROBIOLOGY, vol. 140, no. 1, 1994, pages 123-132, XP002160259 READING GB * the whole document *	1,4-6	
A	--- EP 0 452 596 A (N.V.INNOGENETICS S.A.) 23 October 1991 (1991-10-23) * page 1, line 1 - page 6, line 58; claims 1,2 *	1,4-6	TECHNICAL FIELDS SEARCHED (Int.Cl.7) C12Q
D	& WO 91 16454 A 31 October 1991 (1991-10-31) --- -/--		
The present search report has been drawn up for all claims			
Place of search BERLIN		Date of completion of the search 13 March 2001	Examiner De Kok, A
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons &amp; : member of the same patent family, corresponding document</p>			

EPO FORM 1503 (03.82) (P04C01)



European Patent  
Office

# EUROPEAN SEARCH REPORT

Application Number  
EP 01 20 0037

DOCUMENTS CONSIDERED TO BE RELEVANT				
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)	
D,A	EP 0 395 292 A (T.G.BARRY ET AL.) 31 October 1990 (1990-10-31) * page 3, line 27 - line 52 * * page 4, line 28 - page 5, line 18 * * page 8, line 5 - page 9, line 28 * ---	1,4-6		
D,A	R. FROTHINGHAM ET AL.: JOURNAL OF BACTERIOLOGY, vol. 175, no. 10, 1993, pages 2818-2825, XP002160260 BALTIMORE US * the whole document * ---	1,4-6		
A	R. FROTHINGHAM ET AL.: JOURNAL OF INFECTIOUS DISEASES, vol. 169, no. 2, 1994, pages 305-312, XP002160261 CHICAGO US * the whole document * ---	1,4-6		
A	Y. SUZUKI ET AL.: JOURNAL OF BACTERIOLOGY, vol. 170, no. 6, 1988, pages 2886-2889, XP002160262 BALTIMORE US * the whole document * ---	1,4-6		TECHNICAL FIELDS SEARCHED (Int.Cl.7)
D,A	K.E. KEMPSELL ET AL.: JOURNAL OF GENERAL MICROBIOLOGY, vol. 138, no. 8, 1992, pages 1717-1727, XP002160263 LONDON GB * the whole document * -----	1,4-6		
The present search report has been drawn up for all claims				
Place of search BERLIN		Date of completion of the search 13 March 2001	Examiner De Kok, A	
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons &amp; : member of the same patent family, corresponding document</p>				

EPO FORM 1503 03/82 (P04C01)

**ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.**

EP 01 20 0037

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.  
The members are as contained in the European Patent Office EDP file on  
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

13-03-2001

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9311264	A	10-06-1993	AT 165622 T	15-05-1998
			AU 3148593 A	28-06-1993
			CA 2125141 A	10-06-1993
			DE 69225333 D	04-06-1998
			DE 69225333 T	24-09-1998
			EP 0620862 A	26-10-1994
			ES 2114957 T	16-06-1998
			HK 1006063 A	05-02-1999
			JP 7501699 T	23-02-1995
			LT 1511 A	26-06-1995
			LV 10311 A,B	20-10-1994
			MX 9206974 A	01-06-1993
			US 5753467 A	19-05-1998
WO 9304201	A	04-03-1993	US 5521300 A	28-05-1996
			AT 188743 T	15-01-2000
			DE 69230555 D	17-02-2000
			DE 69230555 T	24-08-2000
			EP 0552358 A	28-07-1993
			JP 6502312 T	17-03-1994
EP 0452596	A	23-10-1991	AT 128189 T	15-10-1995
			AU 658143 B	06-04-1995
			AU 7755091 A	11-11-1991
			CA 2080812 A	19-10-1991
			DE 69113261 D	26-10-1995
			DE 69113261 T	13-06-1996
			DK 525095 T	12-02-1996
			WO 9116454 A	31-10-1991
			EP 0525095 A	03-02-1993
			ES 2080945 T	16-02-1996
			GR 3018388 T	31-03-1996
			HU 63463 A	30-08-1993
			HU 217804 B	28-04-2000
			JP 5504889 T	29-07-1993
			JP 3109599 B	20-11-2000
			US 5536638 A	16-07-1996
			US 5945282 A	31-08-1999
EP 0395292	A	31-10-1990	IE 81145 B	03-05-2000
			AT 150091 T	15-03-1997
			AU 630932 B	12-11-1992
			AU 5365290 A	25-10-1990
			DE 69030131 D	17-04-1997
			DE 69030131 T	17-07-1997
			DK 395292 T	15-09-1997

EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.

EP 01 20 0037

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.  
The members are as contained in the European Patent Office EDP file on  
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

13-03-2001

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0395292 A		ES 2100161 T	16-06-1997
		GR 3023600 T	29-08-1997
		JP 3097059 B	10-10-2000
		JP 3130099 A	03-06-1991
		US 5574145 A	12-11-1996
		ZA 9002924 A	27-02-1991
-----			

EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

**THIS PAGE BLANK (USPTO)**